Federal Court | Cour fédérale

Date: 20101222

Docket: T-1272-97

Citation: 2010 FC 1265

BETWEEN:

MERCK & CO. INC. and
MERCK FROSST CANADA LTD.

Plaintiffs/
Defendants by Counterclaim

and

APOTEX INC. and
APOTEX FERMENTATION INC.

Defendants/
Plaintiffs by Counterclaim

PUBLIC REASONS FOR JUDGMENT
(Confidential Reasons for Judgment issued on December 9, 2010)

SNIDER J.

I. Introduction

A. *Overview*

[1] The subject of this litigation is the drug lovastatin, sold in Canada under the trade name MEVACOR since 1988 by Merck Frosst Canada Inc. (or its successor, Merck Frosst Canada

Ltd. (Merck Frosst), one of the Plaintiffs in this action). MEVACOR was the first commercialized “statin” sold in the Canadian market and is used for the treatment of elevated blood cholesterol. Until January 31, 2001, when the patent expired, MEVACOR was the subject of Canadian Patent No. 1,161,380 ('380 Patent) issued January 31, 1984 to Merck & Co., Inc. (Merck & Co.), the other Plaintiff in this action. Stated briefly, the '380 Patent is a product-by-process patent to lovastatin when made with a micro-organism known as *Aspergillus terreus* (also referred to as *A. terreus*). Merck Frosst sells MEVACOR in Canada under licence from Merck & Co. In these reasons, I will refer to Merck Frosst and Merck & Co., collectively, as “Merck” or the “Plaintiffs”.

[2] In March 1997, Apotex Inc., one of the Defendants in this action, began selling its brand of lovastatin tablets in Canada (Apo-lovastatin). The active pharmaceutical ingredient (API) that remains in dispute in this litigation was made either by Apotex Fermentation Inc. (AFI), the other Defendant in this action, in Winnipeg, Manitoba, or by Qingyuan Blue Treasure Pharmaceuticals Co. Ltd. (Blue Treasure), in China. In these reasons, I will refer to Apotex Inc. and AFI, collectively, as “Apotex” or the “Defendants”.

[3] Merck claims that the Defendants infringed the '380 Patent:

- through the use of infringing API that was made in China and shipped from Blue Treasure to AFI;

- through the “salting” of non-infringing lovastatin with infringing lovastatin;

- through the manufacturing of one batch of infringing API (batch CR0157) in Winnipeg by AFI; and

- with some other small amounts of infringing product made in Winnipeg by AFI.

[4] The Defendants claim that there has been no infringement of the '380 Patent and that, in any event, the '380 Patent is invalid. Further, they argue that Merck & Co. has no standing to bring this action, having assigned all of its interest in the '380 Patent to an affiliate, Merck and Company, Incorporated (MACI).

[5] The application leading to the '380 Patent was filed in Canada on June 11, 1980. According to s. 78.1-78.2 of the present *Patent Act*, R.S.C. 1985, c. P-4, as amended, patent applications filed before October 1, 1989, are to be dealt with under the provisions of the *Patent Act* as they read immediately before that date. Accordingly, references in these reasons to the *Patent Act* [referred to as the *Patent Act* or the *Act*], unless specifically noted otherwise, will be to the *Act* as it stood immediately prior to October 1, 1989.

B. *Summary of issues and conclusions*

[6] Very briefly, although there are a myriad of subsidiary issues, the key questions to be addressed in this proceeding are as follows:

1. Does Merck & Co. have standing to bring this action?

2. Have the Defendants infringed the '380 Patent?

3. Is the '380 Patent valid?

[7] As explained in these reasons, I have concluded that:

1. Merck & Co. has standing to bring this action;

2. The '380 Patent was infringed; and

3. The '380 Patent is valid.

[8] As a result, the claims of the Plaintiffs will be allowed, to the extent described below, and the counterclaims of the Defendants will be dismissed.

[9] Finally, by way of introduction, I note that this trial is subject to a bifurcation order dated November 14, 2003 (Bifurcation Order). Accordingly, the question of damages will be considered in a subsequent proceeding.

C. *Background to this litigation*

[10] For almost ten years after its introduction into the Canadian market, Merck enjoyed its patent for MEVACOR without challenge. In 1993, Apotex Inc. tried to enter the market with a generic version of lovastatin and, to that end, applied to the Minister of Health for a Notice of Compliance (NOC) pursuant to the relevant provisions of the *Patented Medicines (Notice of Compliance) Regulations*, SOR/93-133, as amended by SOR/98-166 [*PMNOC Regulations* or the *Regulations*]. Apotex alleged that it would not infringe the '380 Patent, as it would not be using a process to produce lovastatin that would fall within the scope of the patent.

[11] As permitted by the *Regulations*, in April 1993, Merck filed an application with this Court to prohibit the Minister from issuing an NOC to Apotex Inc. A key feature of the *PMNOC Regulations* is the imposition of a statutory stay upon the filing of an application for prohibition until a determination can be made as to whether the “second person” – in this case, Apotex Inc. – was justified in its claims that its generic drug would not infringe any existing patents. Section 6(1) of the *Regulations*, as they were at that time, automatically prohibited the Minister from issuing an NOC to Apotex Inc. for up to 30 months.

[12] The statutory stay expired on December 1, 1996, without any hearing before the Court on the merits of the prohibition application. Merck Frosst Canada Inc. sought an extension of the stay. In an oral judgment dated March 26, 1997, Justice Rothstein (then a judge with the Federal Court, Trial Division) refused to extend the time period or to issue a prohibition order. An NOC was issued to Apotex Inc. on March 27, 1997.

[13] Following the issuance of the NOC and a series of Court challenges, two actions were commenced:

1. Merck commenced this action against Apotex Inc. and Apotex Fermentation Inc. (AFI) for patent infringement (Court File T-1272-97). The statement of claim was filed on June 12, 1997.

2. By statement of claim filed June 29, 2001, Apotex Inc. seeks compensation from Merck under s. 8 of the *PMNOC Regulations* (Court File No. T-1169-01).

[14] In 2001, Apotex Inc. commenced a third party claim against Biogal Pharmaceutical Works Ltd. (Biogal) in Court File No.T-1272-97. The subject matter of the third party claim was 300 kg of bulk lovastatin acquired by Apotex Inc. from Biogal pursuant to a Supply Agreement. In its third party claim, Apotex Inc. claimed that, in the event that the '380 Patent is held to be valid and infringed, Biogal was liable for any relief that may have been awarded against Apotex Inc. Biogal participated in the T-1272-97 litigation until a settlement was reached among the parties to this litigation. By Court Order dated May 28, 2010, the Plaintiffs' claims against Apotex Inc. and AFI in the Amended Fresh as Amended Statement of Claim and referenced in paragraphs 36 and 67-73 therein relating to lovastatin supplied by Biogal to Apotex Inc. were dismissed.

[15] Both actions were heard together in a trial that commenced on February 1, 2010. These Reasons deal only with the issues in Court File No. T-1272-97 – Merck's claim of infringement

and Apotex's counterclaim of patent invalidity. Separate Reasons for Judgment and Judgment have been issued contemporaneously with these Reasons in Court File No. T-1169-01.

[16] During the 35-day evidentiary phase of this trial, many witnesses appeared, both as expert and fact witnesses. In Appendix A, I have set out a brief overview of the expert and fact witnesses who appeared during the trial and the areas to which they testified. For the expert witnesses, I have set out a very short description of their education and experience in the areas for which this Court found each of them to be qualified. More detailed references to the witnesses' evidence and testimony are contained in the appropriate sections of these reasons.

II. Table of Contents

[17] To assist the reader, the following sets out a Table of Contents for these Reasons with paragraph numbers for each heading

III. Background

A. *The '380 Patent and Statins*

[18] Lovastatin, as made by the process of the '380 Patent, is an example of a medicinally-valuable drug that is produced by a process of fermentation. In very simple terms, the laboratory begins with a micro-organism - in this case, *Aspergillus terreus* – and, through increasingly larger fermentations carried out in very controlled settings, manufactures the API of interest.

[19] The '380 Patent relates to “hypocholesteremic products from the cultivation of a microfungus of the species Aspergillus.” Dr. Antonio Gotto provided very helpful background information on the role of “hypocholesteremic” medications, such as lovastatin, in the treatment of cardiovascular disease. In addition to being qualified because of his stature as a professor of medicine, Dr. Gotto’s experience as a treating physician during the 1970s and 1980s was directly relevant to the matters before me.

[20] Atherosclerosis is a type of cardiovascular disease that occurs when cholesterol and other substances build up in the walls of arterial blood vessels to form plaque. Over time, the build-up of plaque thickens and hardens the arterial walls restricting the flow of blood from the heart. Heart attacks and strokes may follow.

[21] The build-up of plaque is promoted by low density lipoproteins (referred to as LDL or "bad" cholesterol). According to Dr. Gotto, the relationship between reducing "bad" cholesterol and reducing the risk of cardiovascular disease has been known for over 20 years. Thus, a primary goal of medicine is to lower LDL cholesterol. The class of drugs known as "statins" are of great assistance in achieving this goal.

[22] In Dr. Gotto's words (Gotto Expert Report, Exhibit 2, paras. 24, 38):

> It was only with the discovery of statins – starting with lovastatin (MEVACOR®) in the late 1970s – that treatment of elevated cholesterol became much more effective.
>
> . . .
>
> The single most significant discovery to date for the treatment of cholesterol was the discovery of lovastatin in the late 1970s.

[23] Dr. Gotto described how statins work to lower cholesterol. Statins reduce the production of cholesterol by the liver. Specifically, statins block the liver enzyme known as HMG-CoA reductase (hydroxyl-methylglutaryl-coenzyme A reductase); hence, statins are known as HMG-CoA reductase inhibitors. Dr. Gotto made the general comment that "statins changed medical practice" (Gotto Expert Report, Exhibit 2, para. 50). No one disagreed with this opinion.

[24] Lovastatin, as manufactured and sold by Merck (or its predecessors in interest) under the trade name MEVACOR, was the first commercially-available statin.

B. *History of AFI/Blue Treasure Production*

[25] An important part of the story for this litigation is how Apotex Inc. became interested in lovastatin and how Apotex Inc., AFI and the Blue Treasure Joint Venture became involved.

[26] Dr. Bernard Sherman is currently the Chairman and Chief Executive Officer of Apotex Inc., a company that he founded in 1973. During his oral testimony, Dr. Sherman described Apotex Inc. in the following terms:

> It's a pharmaceutical manufacturer, the largest in Canada today. We produce primarily generic pharmaceutical products, but also some innovative products. We have huge dosage form manufacturing facilities. We are vertically integrated. We have chemical plants. We spend enormously on research and development, the largest in Canada, and we have divisions in many countries around the world and factories in many countries, including chemical plants.

[27] Apotex Inc. recognized the significance of the lovastatin market. Dr. Sherman described lovastatin, in 1993, as "one of the biggest selling drugs in the country at the time, close to $100 million a year".

[28] Of particular relevance to this litigation, Dr. Sherman told the Court how his company's version of lovastatin became entangled with a suddenly-changed regulatory regime in 1993. Until 1993, it was possible for a generic company to obtain a compulsory licence to allow it to produce a generic equivalent of a patented medicine. The original intent of Apotex Inc. was to obtain a compulsory licence to use *Aspergillus terreus* to make lovastatin. According to

Dr. Sherman, in 1993, the licence regime and licences issued under it were cancelled. They were replaced with the *PMNOC Regulations* outlined by Dr. Sherman as follows:

> In 1993, not only were the licences – the licence regime eliminated, including retroactive cancellation of some licences – one applicable to this case – but, in addition to that, a new regime was instituted, called the Patented Medicines (Notice of Compliance) Regulations, pursuant to which patentees or first persons, persons who had approval for the original brand, could list patents which they purported were relevant to a product; and, if they listed the patent, then a generic applicant, a second person, cannot get federal approval until the requirements of those regulations are satisfied, which means that the second person has to serve a notice of allegation in which it is alleged that the patent will not be infringed or is invalid. Then, within 45 days, if the patentee or first person institutes a prohibition application, which almost always happens, there is a delay in federal approval until that matter is resolved, which can take a very long time.

[29] A relationship of interest to this case is that of Apotex Inc. and AFI. In the mid-1980s, Apotex Inc. contracted with ABI Biotechnology Inc. (ABI) in Winnipeg to develop and manufacture certain fermented products. Ultimately, the assets of ABI were bought by Apotex Inc. and the company was renamed as AFI. Through AFI, Apotex Inc. gained the capacity to manufacture products using fermentation processes. AFI added to the vertical integration of the Apotex family of business entities.

[30] AFI was to be the source of the API lovastatin. As described in detail by Dr. Lasure, in her Expert Report (Exhibit 48), and by Dr. David Cox, during his testimony, the following steps were taken by AFI:

- AFI acquired Merck's deposited strains of *Aspergillus terreus* from the American Tissue Culture Collection (ATCC), including a strain designated ATCC 20542.

- ATCC 20542 was then mutated by UV mutagenesis twice to create a mutant strain of ATCC 20542.

- AFI designated the strain as BN-2-70 and the process for manufacturing lovastatin using this strain as AFI-1.

- Between 1991 and 1995, AFI developed a commercial scale fermentation process for making lovastatin using AFI-1 – that is, using *Aspergillus terreus*.

[31] In 1992, Dr. Sherman testified that, anticipating the intent of the government, Apotex began to look for a non-infringing process. Apotex “had to find a microbe that would produce lovastatin that was not *Aspergillus terreus*”. In her Expert Report, Dr. Lasure summarized the context and the results of this search:

- On June 25, 1988, the Journal of Antibiotics published an article entitled "The Synthesis of Compactin (ML-236B) and Monacolin K in fungi" written by Dr. Akira Endo et al. Dr. Endo reported on fungal strains capable of producing Monacolin K (known now to be lovastatin), including *Phoma* species M4452.

- In June 1992, a sample of *Phoma* Sp. M4452 was sent to AFI by Dr. Endo.

- For the next six months or so, AFI took steps in its laboratories to confirm and develop the production of lovastatin from the Endo sample. The process was initially referred to as *Phoma* #4; later designated as “AFI-4”.

- By May 1993, a sample of the AFI-4 product was confirmed to be *Coniothyrium fuckelii* (also referred to as *C. fuckelli*).

- Apotex Inc. filed a patent for the AFI-4 process – a process for making lovastatin using *Coniothyrium fuckelii* – that subsequently issued as United States Patent No. 5,409,820 on April 25, 1995.

[32] As described by a number of witnesses, including Dr. Cox and Ms. Lori Christofalos, AFI’s production of AFI-4 lovastatin and shipments to Apotex Inc. can be divided into three phases:

1. Phase 1 occurred between June 1996 and August 1997, during which all production was done solely at AFI facilities in Winnipeg. The finished API was shipped to Apotex Inc., beginning with the shipment of batch CR0157 on December 2, 1996.

2. In Phase 2, Blue Treasure (discussed below) manufactured approximately 70 batches of technical-grade lovastatin. The product was then shipped to AFI for

processing into API and shipment to Apotex Inc. Phase 2 lasted from about mid-1997 to January 1998.

3. Phase 3 consisted of approximately 294 batches of API-grade lovastatin manufactured entirely at Blue Treasure after March 1998.The product was sent to AFI, where “some testing” was carried out, and then shipped to Apotex Inc. This phase continued until October 1999, with the last shipment received at AFI on March 2, 2000.

[33] The joint venture company known as Qingyuan Blue Treasure Pharmaceuticals Co. Ltd. (Blue Treasure or Blue Treasure Joint Venture) is a critical component of this litigation. Dr. David Cox, President and Chief Executive Officer of AFI from September 1994 to September 1997, provided a clear and helpful background about this joint venture. Dr. Cox was on the Board of Directors of Blue Treasure during the same period.

[34] Blue Treasure was formed pursuant to a Joint Venture Contract dated January 25, 1994 among Qingyuan New North River Pharmaceutical Co. Ltd. (New North River), Zuhai Special Economic Zone Lizhu Pharmaceutical Group Co. Ltd., Sichuan Industrial Institute of Antibiotics, AFI and BIOTECS. AFI held a 42.5% share of the Blue Treasure Joint Venture. As set out in clause 4.01 of the Joint Venture Contract, the purpose of the Blue Treasure Joint Venture was as follows:

> The purpose of the Joint Venture is to renovate and operate the Factory, to purchase or otherwise obtain all necessary raw materials and equipment required for the production of the

> Products, and to produce, market, distribute and sell Products at a profit to customers both in China and abroad.

[35] In 1994, New North River was already an operational pharmaceutical facility with capacity for carrying out fermentation processes. Under the Joint Venture Contract, New North River contributed a portion of its facilities located on its property to the Blue Treasure Joint Venture.

[36] As defined in the Joint Venture Contract, “Products” meant “the drug Lovastatin as Bulk Products and Finished Products”. Dr. Cox stated that the Blue Treasure Joint Venture “was set up to produce and distribute and sell Lovastatin in the Chinese domestic market”. AFI’s main contribution to the Blue Treasure Joint Venture was the organism that produced lovastatin. Dr. Sherman told the Court that the decision to move the production of lovastatin to Blue Treasure was made for the following reasons:

> [Blue Treasure] had capacity there, and we wanted to move the production for Canada out of Winnipeg, both to bring costs down and to free up Winnipeg to go on for other things that would be needed later.

[37] In the spring of 1995, AFI transferred to Blue Treasure the information and knowledge it had developed to manufacture lovastatin made from *Aspergillus terreus*. Among the things transferred to Blue Treasure were: a document setting out the process for producing lovastatin from *Aspergillus terreus*, entitled "Scale-up Process to 15000L Fermenter"; and, 25 vials of strain BN-2-70 from seed bank A18-378, and 5 rice cultures from batch #CF0057 (shipped to Blue Treasure on May 15, 1995). Blue Treasure began producing lovastatin, using the AFI-1 process, in 1996.

[38] In about April 1997, AFI determined that it would transfer the AFI-4 technology to Blue Treasure together with a guarantee that AFI would purchase the lovastatin from Blue Treasure, provided that the lovastatin was all made by the AFI-4 process and that "the Blue Treasure facility be exclusively dedicated to AFI-4". The terms of this arrangement were set out in a letter agreement dated April 16, 1997 between AFI and Blue Treasure. Dr. Cox described the impact of the AFI-4 transfer as "transformative in a positive way". The transfer of AFI-4 to Blue Treasure was made with very explicit instructions that the lovastatin purchased by Apotex was to be produced exclusively with the AFI-4 *Coniothyrium fuckelii* strain, with no possibility of contamination from *Aspergillus terreus* (see, for example, letter dated September 12, 1997 from Mr. Fowler to Mr. Zhou). Problems quickly arose. These problems are discussed later in Section VII of these reasons.

[39] From 1997 to 1999, AFI imported lovastatin from Blue Treasure in accordance with the terms of the Blue Treasure Joint Venture. The lovastatin API was then sold to Apotex Inc.

IV. Standing

[40] The first issued raised by Apotex is the standing of Merck & Co. to bring this action.

[41] The authority of a party to claim damages for patent infringement is found in s. 55(1) of the *Patent Act*.

55.(1) Any person who infringes a patent is liable to the patentee and to all persons claiming under him for all damages sustained by the patentee or by any person, by reason of the infringement.	55.(1) Quiconque viole un brevet responsable, envers le breveté et envers toute personne se réclamant du breveté, des tous dommages-intérêts que cette violation a fait subir au breveté ou à cette autre personne.

[42] The term “patentee” is defined in s. 2 of the *Patent Act* to mean “the person for the time being entitled to the benefit of a patent”.

[43] The '380 Patent was granted to Merck & Co. In 1985, Merck & Co. entered into a License Agreement with Merck Frosst (the 1985 License Agreement), granting an non-exclusive licence to Merck Frosst. That Agreement was amended, effective January 1, 1989, to add the '380 Patent. Subsequently, as of January 1, 1992, Merck & Co. entered into an agreement (the MACI Agreement) with Merck and Company, Incorporated (MACI) pursuant to which Merck & Co., as Licensor, granted to MACI, as Licensee:

> A permanent and exclusive royalty-free license for the Intellectual Property which Licensor owns or hereinafter acquires, but for any outstanding licenses for the Intellectual Property which already granted pursuant to the License Agreement, dated January 1, 1985, and amendments thereto between Merck & Co., Inc. and Merck Frosst Canada Inc.

[44] Apotex does not dispute Merck Frosst Canada Ltd.’s standing in this action, as the successor in interest to Merck Frosst Canada Inc. However, Apotex submits that Merck & Co. has no standing to bring this action, having assigned all of its interest in the '380 Patent to MACI

pursuant to the MACI Agreement. Apotex asserts that, as of November 1992, MACI had the "full and unrestricted benefit of the '380 Patent". Merck & Co. lost all benefit of the patent and, as a result, the right to damages under s. 55 (1) of the *Patent Act*. Apotex argues that, although the agreement is entitled "License Agreement", a review of the words of the agreement demonstrates that the intent of the parties to the MACI Agreement was to convey the entire right, title and interest in the '380 Patent to MACI.

[45] Apotex submits that agreements which take the form of a licence, but nevertheless convey all of the substantive rights in a patent, have consistently been held to constitute an effective assignment or transfer of that patent. In support of this argument, Apotex relies on a line of jurisprudence of courts in the United States and the United Kingdom (*Merck & Co., Inc. v. Francis R. Smith*, 261 F.2d 162 at 164 (3rd Cir. 1958); *Vaupel Textilmaschinen KG v. Meccanica Euro Italia SPA*, 944 F.2d 870, 874 (Fed. Cir. 1991); *Prima Tek II, L.L.C. v. A-Roo Co.*, 222 F.3d 1372, 1377-78 (Fed. Cir. 2000); *Guyot v. Thompson* [1894] R.P.C. 541 at 554 (C.A.)[*Guyot*]).

[46] I do not find the authorities relied on by Apotex to be of any assistance. Except in the case of *Guyot*, above, a decision of the High Court of Justice – Chancery Division, the Courts in those cases were considering the effect of agreements in the context of U.S. patent law. I do not see how they could guide this Court in determining the meaning of the terms of and, if necessary, the intent of the parties to the MACI Agreement. I did not have the benefit of an expert in U.S. law opining as to whether the MACI Agreement would constitute a transfer of all of the rights of the patent to MACI under applicable U.S. law. Moreover, the facts in *Guyot*, where an exclusive

assignee was attempting to enforce the terms of an Indenture, are simply too remote from the question before me.

[47] Rather, I would look at this issue in the context of the Canadian law of contracts. As I understand the state of the Canadian law of contracts, the express language of the parties to a contract is the core of their contractual obligations. Where the words of a contract are clear and unambiguous, a court need not look beyond those clear words to determine its intent and effect.

[48] Apotex was unable to point me to a single Canadian case that supports its position. Nevertheless, I would agree that the title of the License Agreement would not be determinative if there is clear and persuasive evidence that Merck & Co. intended to convey all of its rights in the '380 Patent to MACI, retaining nothing to itself. Whether this is so or not will depend on an examination of the words of the MACI Agreement and the facts and circumstances surrounding the MACI Agreement.

[49] In this case, the express language of clause 2 of the MACI Agreement uses the word “license”. On its face, the MACI Agreement only grants a “license”. The Supreme Court of Canada in *Domco Industries Ltd., v. Armstrong Cork Canada Ltd.*, [1982] 1 S.C.R. 907 at p.912, 66 C.P.R. (2d) 46, adopted the comments of Fry L.J. at p. 470, in *Heap v. Hartley* (1889), 42 Ch. D. 461:

> An exclusive license is only a license in one sense; that is to say, the true nature of an exclusive license is this. It is leave to do a thing, and a contract not to give leave to anybody else to do the same thing. But it confers like any other license, no interest or property in the thing. [Emphasis added.]

[50] I also note the language of certain clauses in the MACI Agreement that refer to rights retained by Merck & Co. For example, clause 3 provides the Licensor with the rights to inspect the Licensee's facilities. Under clause 5.2, the Licensee is to supply the Licensor with a detailed description of any disclosure of "licensed know-how" to any governmental authority. In my view, retention of rights such as these is inconsistent with an intention to transfer all rights under the patent.

[51] In support of its position, Apotex points to a recital to the MACI Agreement:

> WHEREAS, the Licensor desires to grant the Licensee a permanent and exclusive license with respect to its remaining right, title and interest in and to the rights which it has acquired with respect to such intellectual property as a contribution to the capital of the Licensee. [Emphasis added.]

Apotex relies on the Supreme Court of Canada decision in *Dukart v. Surrey (District)*, [1978] 2 S.C.R 1039 at p.1052-53, 86 D.L.R. (3d) 609 [*Dukart* cited to S.C.R] as support for its submission that, where the words of a recital manifest a clear intention, the Courts have inferred that the parties intended that these words be given effect.

[52] The case of *Dukart* does not assist Apotex. *Dukart* involved the grant of an "easement" and the question of the true intentions of the parties. In that case, the body of the agreement contained no language with respect to the extent of the rights granted under the agreement. The recital clause was used by the Supreme Court to provide the necessary meaning to the agreement.

[53] The case before me is different in that provisions in the body of the MACI Agreement speak to the intent of the agreement and the scope of the "transfer" from Merck & Co. to MACI.

The use of a recital or preamble as an interpretative aid must always be approached with caution. As pointed out by Justice Abella (as she then was) in *Lay v. Lay* (2000), 47 O.R. (3d) 779, 184 D.L.R. (4th) 652 (Ont. C.A.) at paragraph 12, leave to appeal to SCC refused, [2000] S.C.C.A. No. 369 (QL), 264 N.R. 398 (note):

> There is no doubt that an introduction or a preamble can provide interpretative assistance, but I see no basis for accepting the novel proposition that its terms can triumph over those in the body of the contract.

[54] In my view, the words of the MACI Agreement establish the creation of a licence and not a conveyance of all rights in the '380 Patent. The use of the word “remaining” in the recital does not “triumph over” the words of the agreement. This is sufficient to defeat the argument of Apotex.

[55] However, even if I accept that there may be ambiguity in the MACI Agreement, I am satisfied that the parties to the MACI Agreement did not intend to convey the entire right, title and interest in the '380 Patent. One indication of the intent of the parties to an agreement is the behaviour of the parties. If the MACI Agreement is not clear on its face, it is of assistance to examine the behaviour of the parties after the execution of the agreement. Was the behaviour of Merck & Co., from November 1992, consistent with a company who had given up its entire right, title, estate and interest in the '380 Patent? Clearly, the answer is “no”. If there had been such intent, why would Merck & Co. commence and pursue this litigation for 13 years in its own name? Further, why would Merck & Co. remain as the named patentee on the '380 Patent?

[56] I am satisfied that the MACI Agreement did not operate as a conveyance of the entire right, title and interest of Merck & Co. to MACI. Merck & Co. has standing to bring this action.

V. Claims Construction

A. *Principles of Claims Construction*

[57] The first step in a patent suit is to construe the claims, in accordance with principles that are well-established in the jurisprudence (see, for example, *Whirlpool Corp. v. Camco Inc.*, 2000 SCC 67, [2000] 2 S.C.R. 1067 [*Whirlpool*]). This jurisprudence teaches that claims are to be interpreted in a purposive way in order "to achieve fairness and predictability and to define the limits of the monopoly" (*Dimplex North America Ltd. v. CFM Corp.*, 2006 FC 586, 292 F.T.R. 38 at para. 49 [*Dimplex*], aff'd 2007 FCA 278, 60 C.P.R. (4th) 277).

[58] Construction of the claims is a matter for the Court to determine. The Court is called on to determine, on an objective basis, what a hypothetical skilled person would have understood the invention to mean (*Whirlpool*, above, at paras. 45, 53). Where a patent is of a highly technical nature, the person skilled in the art will be someone possessing a high degree of expert scientific knowledge in the particular field of art to which the patent relates (*Aventis Pharma Inc. v. Apotex Inc.*, 2005 FC 1283, 278 F.T.R. 1 [*Ramipril I (FC)*]; *Apotex Inc. v. Syntex Pharmaceuticals International Ltd et al* (1999), 166 F.T.R. 161 at para. 38, [1999] F.C.J. No. 548 (QL)(F.C.T.D.).

[59] Where necessary, the whole of the patent, and not only the claims, should be interpreted (*Eli Lilly Canada Inc. v. Apotex Inc.*, 2008 FC 142, 63 C.P.R. (4th) 406 at para. 25; *Eli Lilly Canada Inc. v. Novopharm Ltd.*, 2007 FC 596, 58 C.P.R. (4th) 214 at para. 103). The Court should construe the claims in light of the description in the specification, assisted by experts as to the meaning of technical terms if such terms cannot be understood by the Court from reading the specification (*Shire Biochem Inc. v. Canada (Minister of Health),* 2008 FC 538, 328 F.T.R. 123 at para. 22 [*Shire*]; *Whirlpool*, above, at para. 45).

[60] It is also important to recognize that purposive construction should be directed at the points in dispute between the parties (*Shire*, above, at para. 22).

[61] Lastly, as the '380 Patent was issued under the old *Patent Act*, all claims at issue are to be construed as of the date the patent was granted and issued (*Pfizer Canada Inc. v. Canada (Minister of Health),* 2005 FC 1725, 285 F.T.R. 1 at para. 36). For the '380 Patent, that date is January 31, 1984.

[62] With these overarching principles in mind, I turn to the patent in question.

B. *The hypothetical skilled person*

[63] As noted, claims must be construed from the view of a hypothetical skilled person. Thus, as a preliminary matter, I must define what attributes would be held by our hypothetical skilled person.

[64] In its final written argument, Apotex described the person to whom the '380 Patent is addressed as follows:

> The skilled addressee of the ’380 Patent is a notional person having a thorough knowledge of cultivating fungal micro-organisms. Such a person may have an advanced degree, such as a Ph.D., in biochemistry, mycology or industrial biochemical processes and several years of related practical experience in an industrial setting. The skilled addressee would also include pharmaceutical formulators, and medical and organic chemists interested in using the compounds of the alleged invention to treat hyperlipemia and hypercholesteremia.

[65] Given the nature of this product-by-process patent, I believe that experience and knowledge related to fungal micro-organisms is fundamental. This expertise would, in my view, include both academic qualifications and technical experience. Identification of micro-organisms, developing, recognizing and identifying productive strains and growing cultures in appropriate media for commercialization are all aspects of the '380 Patent with which the skilled addressee must be familiar. I agree with Dr. Clardy when he states (Clardy Expert Report, Exhibit 17, para. 25):

> … [F]ermenting fungi to obtain secondary metabolites requires experience beyond ordinary academic training and because isolating natural products from fermentations requires the interplay of chemistry, biosynthesis and biological assays beyond formal academic training.

[66] Since the invention consists of processes for preparing compounds that are targeted to lower serum cholesterol, the skilled person would have sufficient knowledge of medical and organic chemistry to be able to understand cholesterol biosynthesis. This expertise could be acquired through academic training or clinical practice.

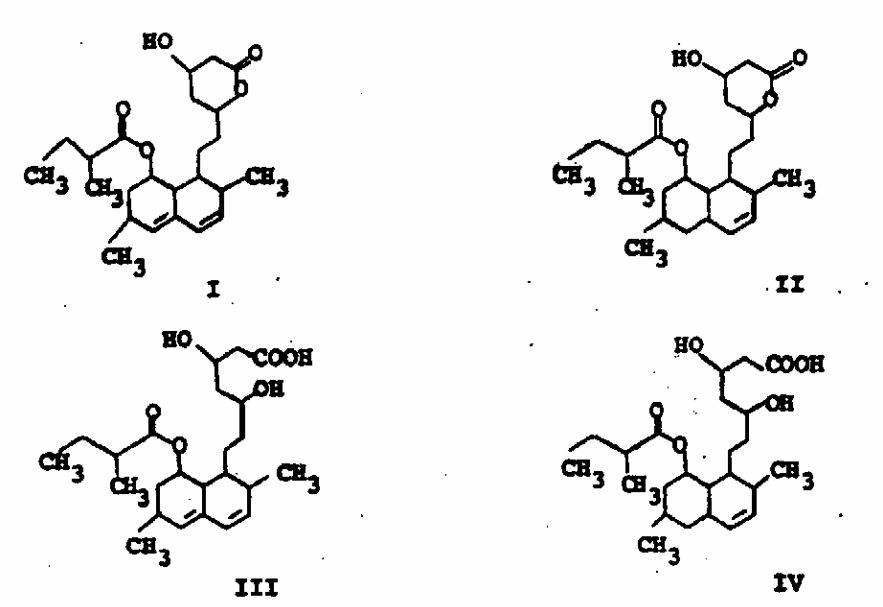
[67] With these remarks on some of the skills necessary, I accept Apotex's description of the person to whom the '380 Patent is addressed.

C. *The Patent Specification*

[68] I begin with a brief overview of the patent specification.

[69] The '380 Patent is what is commonly described as a product-by-process patent. That is, the inventors do not make a specific (or *per se*) claim to the compound lovastatin; rather, they claim the product lovastatin and three other compounds when the compounds are made by the processes described in the patent. The '380 Patent is entitled "HYPOCHOLESTEREMIC FERMENTATION PRODUCTS AND PROCESS OF PREPARATION". As set out in the summary:

> This invention relates to hypocholesteremic products from the cultivation of a microfungus of the species Aspergillus. More specifically, it relates to compounds of the formulae:



> as well as pharmaceutically acceptable salts and lower alkyl and substituted alkyl esters of the carboxylic acids in which the possible substituent is phenyl, dimethylamino or acetylamino. The invention also relates to a process of cultivating the microfungus and isolating from the medium a hypocholesteremic compound of the above structures. These new compounds have excellent properties of inhibiting cholesterol biosynthesis and are useful against hypercholesteremia and hyperlipemia.

[70] I was assisted in understanding the chemical structures of, and relationship amongst, the four compounds identified in this summary (and set out in claim 1) by Drs. Lasure, Clardy and Samson.

[71] Compound I is the marketed product named lovastatin. Compound II is dihydro-lovastatin. It differs from lovastatin (Compound I) only in relation to the bonds in the double ring structure. Compounds I and II are both lactones, meaning that the ring at the top right of the structure is closed. Compound III is the open acid or hydroxy acid form of Compound I and Compound IV is the open acid or hydroxy acid form of Compound II. Each of Compounds III and IV has an open ring at the top with a COOH (carboxyl) group.

[72] At p. 2 of the patent description, the inventors disclose, as prior art, the work and patents of Endo and others related to the compound compactin:

> Recently, Endo et al., described (U.S. 4,049,495 and 3,983,140) a fermentation product obtained by cultivation of a micro-organism of the genus Penicillium and isolation from the medium. They called it ML 236 B and determined its structure together with two related compounds 236 A and 236 C. Its structure, under the name compactin, was also determined by A.G. Brown, T.C. Smale, T.J. King, J. Chem. Soc. (Perkin I) 1165 (1975). This compound has been found to be an inhibitor, in vivo, of the biosynthesis of cholesterol.

[73] The inventors then distinguish their invention from that of the prior art.

> We have found that unexpectedly, the cultivation of a micro-organism very different from that employed by Endo, a microfungus of the genus Aspergillus, produces new substances that are also very potent inhibitors of the biosynthesis of cholesterol in mammals. We have further found that these substances comprise principally the new compounds I, II, III and IV, of the above structures, accompanied by only traces of other compounds. These new compounds are much more potent inhibitors of cholesterol synthesis in vivo than is the compound, ML236B described by Endo.

[74] In short, the patent specification discloses that the inventors of this patent built on the existing work of Endo and others in relation to the anti-cholesterol properties of compactin. They discovered that the Compounds I, II, III and IV, cultivated from "a microfungus of the genus *Aspergillus*", rather than from the genus *Penicillium*, were more potent inhibitors of cholesterol synthesis *in vivo* than compactin.

[75] At p. 3 of the patent specification, the inventors state that, "The compounds of this invention are highly useful as antihypercholesteremic agents for the treatment of atherosclerosis, hyperlipemia and like diseases in humans."

[76] Beginning on p. 4, the inventors begin their more detailed description of how this invention relates to a process for producing the identified compounds. From the experts, I have learned that the method of production of the '380 Patent is described as a "fermentation". Dr. Lasure described this as follows (Lasure Expert Report, Exhibit 48, para. 20):

> Unlike more traditional processes by which chemists may synthesize chemical compounds in a laboratory or a factory using controlled chemical reactions in vitro, the process disclosed in the '380 Patent is a biological process involving the use of a specific

> fungus that synthesizes lovastatin in vivo when that fungus is grown in or under certain conditions which the ‘380 Patent calls a “fermentation”.

[77] The inventors describe their use of two sample micro-organisms from the culture collection of Merck and Co., referred to as MF-4833 and MF-4845. These two micro-organisms were placed on deposit with the American Type Culture Collection (ATCC) and assigned accession numbers ATCC 20541 and ATCC 20542 respectively. It is clear that the inventors are not limiting their invention to the use of these two micro-organisms.

> Although the use of these is described in connection with the process of this invention, other organisms of the genus Aspergillus including mutants of the above ones are also capable of producing these novel compounds and their use is contemplated in carrying out the process of this invention.

[78] In the paragraph that follows, the inventors disclose that:

> The morphological characteristics of the micro-organisms MF-4833 and MF-4845 have been found to be those of the genus Aspergillus. Using the criteria specified in the standard authority . . . and by comparison with known species, it has been determined that both strains are Aspergillus terreus.

[79] Beginning at the bottom of p. 5, the process of fermentation is described, with reference to such matters as illustrative media, optimal temperature ranges and the pH of nutrient media suitable for growing the culture. More detail is provided regarding fermentation scaling, from the initial culture in small flasks to the large-scale fermentation tanks. Once the fermentation broth is made, the reader is instructed that the compounds are conveniently isolated from the fermentation broth as lactones I and II or, alternatively, as salts of Compounds III and IV. Other methods of yielding the compounds of the invention are disclosed.

[80] The physico-chemical properties of the compounds are set out starting at p.8. At p. 9-10, the inventors set out their belief, “with a considerable degree of certainty”, the stereo chemical structures of Compounds I and III. Similar data and stereo chemical structures of Compounds II and IV are described at p. 11-12.

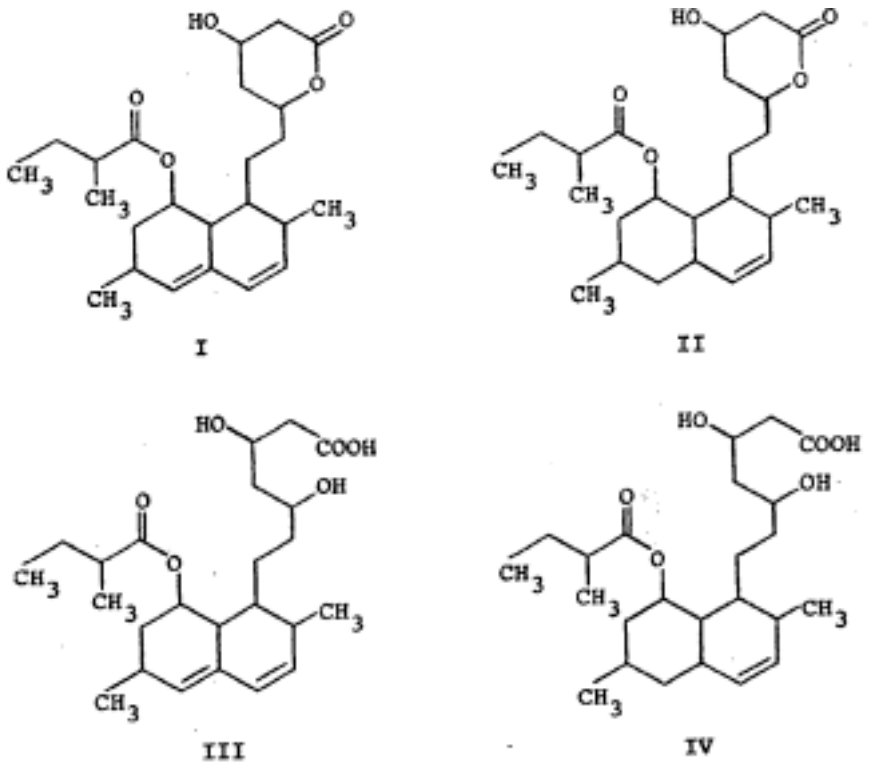
[81] The specification, from p. 13 to 43, illustrates the “invention” with 27 examples.

D. *The claims in issue*

[82] Merck, as it outlined in a response to a demand for particulars dated July 8, 1998, alleged that claims 1 to 8, 10, 11, 13 to 16, 18 and 19 of the '380 Patent were infringed by the Defendants. Merck specifically stated that it was not relying upon every claim in the '380 Patent.

[83] In their Statements of Defence and Counterclaim, Apotex asserts that all of the claims of the '380 Patent are invalid. Subsequent submissions of the parties lead me to the conclusion that, at this stage, the only claims still in issue – and that require construction – are claims 1 to 8 and

13 to 15. I have set out claim 1 in full below. The remaining claims are included in Appendix B to these reasons.

> 1. A process of producing the compounds of structural formulae:
>
> 
>
>
> which compromises fermenting a nutrient medium with a microorganism of the genus *Aspergillus terreus* and isolating the products and when desired converting said products to their corresponding pharmaceutically acceptable salt or lower alkyl ester or a substituted lower alkyl ester wherein the substituent is phenyl, dimethylamine or acetylamine or the cation of the salt is derived from ammonia, ethylenediamine, N-methyl-glucamine, lysine, arginine or ornithine.

[84] The disagreement between the parties focuses on aspects of claim 1. The proper construction of the other claims at issue flow from a resolution of the construction of claim 1. That is, a proper construction of claim 1 will be determinative of the main points in dispute for the remainder of the claims in issue, claims 2 to 8 and 13 to 15.

[85] The areas of disagreement between Apotex and Merck are the following:

1. What is the meaning of the phrase “a micro-organism of genus *Aspergillus terreus*” in claim 1?

2. What is the meaning of the word “isolating” in claim 1?

3. Does the '380 Patent promise that all strains of *Aspergillus terreus* will be capable of producing the four compounds of the invention?

4. What is the promised use of the claimed invention?

[86] The final two construction issues relate to the “promise” of the '380 Patent. The question of what is promised – or not – by the '380 Patent is primarily relevant to the question of the utility of the patent. However, it is an analysis that logically forms part of the '380 Patent claims construction.

[87] Generally, ascertaining the promise of a patent is an exercise that requires the assistance of expert evidence (*Bristol-Myers Squibb Co. v. Apotex Inc.*, 2007 FCA 379, F.C.J. No. 1579 (QL) at para. 27). This is because the promise should be properly defined, within the context of the patent as a whole, through the eyes of a person of skill in the art.

E. *The meaning of "a microfungus of genus Aspergillus terreus" in claim 1*

[88] The first construction issue raised by Apotex relates to the proper interpretation of the words "a micro-organism of the genus *Aspergillus terreus*" in claim 1.

[89] Claim 1 speaks to a process for producing four compounds "which comprises fermenting a nutrient medium with a micro-organism of the genus *Aspergillus terreus* . . .." Apotex argues that, on a proper interpretation of claim 1, a skilled person would read the words "genus *Aspergillus terreus*" as referring to all micro-organisms in the genus *Aspergillus*. Merck asserts that claim 1 is limited to micro-organisms of the species *Aspergillus terreus*.

[90] The nomenclatures used in the '380 Patent would be understood by any high school biology student (and even this judge) as part of the binomial system of naming living organisms. All living

organisms are named according to a hierarchy of classifications. The hierarchy is as follows:

(i) Kingdom
(ii) Phylum
(iii) Class
(iv) Order
(v) Family
(vi) Genus
(vii) Species

In accordance with the accepted binomial convention, living organisms are identified by using the name of the genus (capitalized) together with the name of the species within the genus (lower case).

[91] There is no such genus as *Aspergillus terreus*. As I have learned from the experts in this case, Drs. Clardy, Lasure and Samson, the well-established rules of taxonomy dictate that *Aspergillus* is a genus and that *Aspergillus terreus* is a species within the genus *Aspergillus*. As submitted by the parties, the use of the term "genus *Aspergillus terreus*" in claim 1 can mean one of two things:

(a) the inventors were claiming only those compounds made with micro-organisms of the species *Aspergillus terreus*, and inadvertently used the term "genus" in place of "species" (Merck's position); or,

(b) the inventors were claiming compounds produced from any micro-organism falling within the genus *Aspergillus* (Apotex's position).

[92] Even without expert assistance, it appears to me that the first option provides the preferable interpretation. There is no question that the skilled reader would recognize *Aspergillus terreus* as a species – that is, a subset of the genus *Aspergillus*. The skilled reader would assume that the inventors intended that claim1 include only the micro-organisms of the genus *Aspergillus* that belong to the species *terreus*. To read the phrase as including all species within the genus *Aspergillus* would ignore the plain meaning of the term *terreus*, as used in the claim.

[93] Not only does my construction of the words accord with common sense, it is consistent with the opinions of Drs. Lasure and Clardy. In the view of Dr. Clardy (Clardy Expert Report, Exhibit 17, para. 33):

> … [T]he words *Aspergillus terreus* were in January 1984 and remain today words which, by definition, mean and would be read by the skilled person to describe a subset or sub-category of *Aspergillus* that is not and cannot include the entire *Aspergillus* genus.

[94] Initially, Dr. Samson expressed a different interpretation of this phrase and concludes that (Samson Expert Report, Exhibit 109, para. 37):

> … [B]ased on the repeated references in the patent to the use of a micro-organism of the "genus *Aspergillus*" and from the balance of my review of the '380 Patent described above, it is my opinion that a person skilled in the are would have concluded that the inventors did not intend to place any limits on the micro-organisms that can be used in the process other than that they be from the genus *Aspergillus*.

[95] I acknowledge that the disclosure or specification of the '380 Patent makes a number of references to the "genus *Aspergillus*". Nevertheless, the key problem with Dr. Samson's interpretation of the phrase "genus *Aspergillus terreus*" in claim 1 is that it ignores completely the word "*terreus*". If I were to accept Dr. Samson's opinion, I would be expanding the claim from "*Aspergillus terreus*" to the much broader designation of "*Aspergillus*". As Dr. Samson stated, there are over 250 species that fall within the genus *Aspergillus* (Samson Expert Report, Exhibit 109, para. 17).

[96] Dr. Samson's approach to claims construction is contrary to the teachings of the Supreme Court in *Whirlpool*, above, at paragraph 52, where Justice Binnie refers to the statement of Taschereau J. in *Metalliflex Ltd. v. Rodi & Wienenberger AG* (1960), [1961] S.C.R. 117 (S.C.C.), at p. 122:

> The claims, of course, must be construed with reference to the entire specifications, and the latter may therefore be considered in

> order to assist in apprehending and construing a claim, but the patentee may not be allowed to expand his monopoly specifically expressed in the claims "by borrowing this or that gloss from other parts of the specifications". [Emphasis added.]

[97] During cross-examination, Dr. Samson appeared to have qualified or changed his opinion. Specifically, he agreed that "the inclusion of the word '*terreus*' in claim 1 excludes all other species of *Aspergillus* including *niger* and *nidulus* and *oryzae* and the other 246 [species]."

[98] Moreover, when read in its entirety, the specification is consistent with the limitation of the invention to micro-organisms of the species *Aspergillus terreus*. For example, the inventors disclose the use of micro-organisms MF-4833 and MF-4845; these are examples of *Aspergillus terreus* and not of some other species within the genus *Aspergillus*.

[99] In summary on this point, the words of claim 1 make it very clear that the patentee is not claiming compounds made with any of the 250 species of *Aspergillus*; rather, the boundary of the invention, as claimed, includes the four identified compounds when made with a single species – *Aspergillus terreus*. The use of the word "genus" before "*Aspergillus terreus*" may have been a simple inconsequential error by the drafters or the patentee may have intended the word "genus" to modify only the word "*Aspergillus*" and not the entire phrase "*Aspergillus terreus*". Regardless, given the specificity of the term "*Aspergillus terreus*", the use of the word "genus" would not change the meaning ascribed to the phrase by the skilled addressee.

F. *The meaning of "isolating the products"*

[100] The second construction issue concerns that part of claim 1 which states that the process of producing the compounds "comprises fermenting a nutrient medium with a micro-organism of the genus *Aspergillus terreus* and isolating the products . . .".

[101] The parties disagree on the meaning of the phrase "isolating the products". Apotex submits that claim 1 requires the production of all four of the compounds, that claim 2 requires the production of both Compound I and II (the lactones) and that claim 5 requires the production of both Compound III and IV (the hydroxy acids). In other words, Apotex argues that, for purposes of the claims, the compounds must be separated from each other, purified and crystallized before they are "isolated". Merck submits that "isolating" simply means separating the compounds from the fermentation broth and does not require the compounds to be purified or crystallized.

[102] The term "isolating" is not defined in the patent. Therefore, it is necessary to review the specification to determine what meaning was reasonably intended by the inventors.

[103] Example 1 of the '380 Patent is entitled "Preparation of Compounds I and III". The inventors first set out a procedure for fermenting a particular culture of *Aspergillus terreus*. At the end of this step, the skilled person would have a fermentation broth that is "set aside for isolation of the product". After the fermentation is completed, the next step is the "Isolation of Compound I". This involves separating the broth solids from the broth liquids, extracting the

liquids using a mixture of solvents and extracting the solids. The resulting extracts are combined and concentrated to 15 ml of crude extract. There is no purification or crystallization described as part of the “Isolation of Compound I”. Further, the next step – “Testing of Compound I” – is carried out on the crude extract. There is no further purification or crystallization carried out before the testing.

[104] In reviewing the examples of the patent, I note that Examples 3, 4 and 5 all refer to isolation without any purification or crystallization.

[105] From the specification, I conclude that the inventors meant the term “isolating” to simply refer to separating the compounds from the broth. This was the interpretation given to the term “isolating” by Dr. Clardy who opined that (Clardy Expert Report, Exhibit 17, para. 102):

> In the ‘380 Patent "isolating" does not necessarily require complete separation or purification of the active compounds. The concept of "isolating the products" of a fermentation as those words are used in the patent requires getting the products out of the fermentation broth. The products do not necessarily have to be isolated from one another nor be crystalline, nor be completely purified. All of this would be understood by the skilled person reading the patent in January 1984. I note that the "Isolation of Compound I" in Example 6 is more complex and includes the further purification and crystallization of a specific fraction containing Compound I, but example 1 makes clear that such steps are optional and not necessarily required for "isolating" as that word is used in the patent.

[106] Dr. Samson provided a contrary view. In his Reply Expert Report, Dr. Samson opines as follows (Samson Reply Expert Report, Exhibit 11, para. 41):

> The '380 Patent says that the compounds are extracted or isolated from the fermentation broth as “hypocholesteremic compounds” (see page 2, lines 4 to 7). This would have been understood by a

> person skilled in the art to mean that the invention requires that the compounds be removed from the fermentation broth and isolated from any other compound in the broth, and then purified and crystallized so that they can be useful as “hypocholesteremic compounds”.

[107] I have difficulty with Dr. Samson’s understanding of the term “isolating”. Foremost, this interpretation ignores much of the content of the specification that describes the testing of the crude extract. During cross-examination, Dr. Samson acknowledged that, in some of the examples, there was no purification, separation or crystallization prior to testing. Nevertheless, he clung – unreasonable, in my view – to the opinion that the skilled person would presume that “isolation” or “isolating” includes the steps of extraction, crystallization and separation.

[108] Beyond the disclosure of the '380 Patent, the interpretation proposed by Merck is also supported by the reading of claim 1 in the context of the other claims – in particular claim 13. The general process is set out in claim 1. Claim 13 is a claim to a compound selected from Compounds I, II, III and IV. Had the inventors intended claim 1 to require a separation of each compound from the others, they could have used similar language of selection. The use of the phrase “isolating the products” rather that “isolating each product” is a strong indication, for the skilled reader, that the inventors did not intend that each of the compounds be separated from each other, purified and crystallized.

[109] In sum, I am satisfied that, on a proper claims construction, the words “isolating the products” in claim 1 do not require that the relevant compounds be separated from each other, purified or crystallized prior to testing.

G. *Inclusion of non-producing strains*

[110] For the third construction question, Apotex submits that, whether the Court construes the phrase “genus *Aspergillus terreus*” in claim 1 to include all micro-organisms or fungi within the genus *Aspergillus* or just those within the species *Aspergillus terreus*, the '380 Patent promises that all such micro-organisms can be used to produce the compounds in the Patent. Merck, on the other hand, asserts that the person skilled in the art would know – and eliminate from coverage of the '380 Patent – any strain or fungus that cannot produce the claimed compounds.

[111] Neither claim 1 nor the specification explicitly states that the '380 Patent excludes non-producing strains of *Aspergillus terreus*. The question to be determined is whether the skilled addressee, in 1984, would know that the claims of the '380 Patent are limited to the producing strains of *Aspergillus terreus*.

[112] An essential element of the invention embodied in the '380 Patent is the production of particular compounds through the process of fermentation or cultivation of fungi. As described by Dr. Lasure, who has extensive experience working with such micro-organisms, “a culture of *Aspergillus terreus* is a living sample of a fungus from that species” (Lasure Expert Report, Exhibit 48, para. 60). Thus, within species, there are variations.

[113] Dr. Sorensen described the organic compounds that are produced by fungi as “secondary metabolites”. “Secondary metabolites” are compounds produced as a result of the metabolic function of the initial fungal micro-organism during the fermentation process (Sorensen Expert

Report, Exhibit 132, para. 6). While Dr. Clardy opined that "in the general case it was expected that a particular isolate from a producing species would be expected to produce a given metabolite," he cautioned that there is always a possibility of non-production, for a number of reasons, all of which would have been known in 1984 (Clardy Expert Report, Exhibit 17, paras. 39-41):

- fungi can be intentionally mutated to disrupt the genes responsible for making a metabolite;

- fungi can lose a producing ability over time because of subculturing, or mishandling, or reasons that are never understood;

- some fungi in a producing species simply do not have production capability, although Dr. Clardy thought that this would be unusual except where the isolates have been maintained by serial subculturing;

- fungi tend to change randomly, especially when stored and maintained artificially by scientists;

- if during subculturing, a sample of a variant is taken for further growth, and especially if there is repeated subculturing, the fungus can become one in which a characteristic of the parent culture is lost; and

- physical deterioration of the fungus will lead to loss of specific metabolic functions.

[114] Dr. Clardy summed up the situation as follows (Clardy Expert Report, Exhibit 17, para. 42):

> It was part of the common knowledge of the skilled person in 1984 and such a person would have known, with virtual certainty, that among the many isolates (or strains) of a given species there would inevitably be found isolates that have lost the capacity to produce a particular metabolite under particular conditions, or in some rare cases, that never had an ability to produce the metabolite at all.

[115] Dr. Samson did not share this opinion. In his view, the skilled person would interpret the claims as including the production by *Aspergillus* of all four identified compounds (Samson Expert Report, Exhibit 110, para. 52). He disagreed that the exclusion of non-producing strains was implicit. However, during cross-examination, he acknowledged that the opinions of Drs. Lasure and Clardy were "both scientific opinions that a reasonable person of ordinary skill in the art could have reached in January 1984".

[116] Dr. Samson, during cross-examination, also agreed that the person of ordinary skill in 1984 would have been fully aware that not every strain in a species will make a given metabolite. Even more specifically, Dr. Samson acknowledged that, in 1984, a skilled person reading the claims of the '380 Patent would know that there are strains of *Aspergillus terreus* that would not produce lovastatin.

[117] In sum, I prefer the opinions of both Drs. Lasure and Clardy to the effect that a skilled person would know, from his or her general knowledge, that:

(a) there are many variations in the micro-organisms within the species *Aspergillus terreus*, such that not every micro-organism within the species will necessarily provide the desired results and that some testing and routine experimentation will be required; and

(b) the term “nutrient medium”, as used within the patent description, would include the media used in the examples and other media that, upon routine testing, would result in the desired compounds.

[118] In light of this general knowledge, Drs. Clardy and Lasure were both of the opinion that the skilled person would recognize – even without an explicit limitation in the claims – that the claims of the '380 Patent exclude non-producing strains of *Aspergillus terreus*. The use of the word “producing” in claim 1 tells the skilled person that non-producing strains are excluded, even though the explicit words are not used.

[119] Further support for the conclusion reached by Drs. Clardy and Lasure is contained within the disclosure. In addition to the disclosure of the structure of the compounds and the therapeutic activity of the compounds, the skilled person is provided with examples of the media and conditions that could be used.

[120] Moreover, the skilled person would also bring to his or her laboratory “bench”, a set of skills used routinely. In light of the nature of fungi and their use in the pharmaceutical industry, it appears logical to me that the skilled person would have extensive experience with the types of experimentation and testing that are used to identify and optimize producing micro-organisms. During cross-examination, Dr. Samson confirmed that a number of experiments, known in 1984, could have been performed simultaneously, in a short period of time, to identify the producing micro-organisms. He agreed that about 300 shake flask experiments could be run at one time. The skilled person could rapidly screen a large numbers of isolates of *Aspergillus terreus* to determine which strains are producing. Moreover, since, on my construction, the claims are limited to strains of the species *Aspergillus terreus*, there are manageable boundaries on the testing that would be required.

[121] Having considered the evidence of the three experts, I am persuaded that the opinions of Drs. Lasure and Clardy on this point are to be preferred to that of Dr. Samson. An implicit requirement that non-producing strains are excluded from the coverage of claim 1 is “being neither benevolent nor harsh but rather seeking a construction which is reasonable and fair to both patentee and public” (*Consolboard Inc. v. MacMillan Bloedel (Saskatchewan) Ltd.*, [1981] 1 S.C.R. 504 at p.520, 56 C.P.R. (2d) 145 [*Consolboard* cited to S.C.R.]). I do not accept Apotex’s assertion that the '380 Patent states, implies or promises that all strains of *Aspergillus terreus* will be capable of producing the four compounds of the claimed invention.

H. *The promised use of the '380 Patent*

[122] As a final construction issue, Apotex submits that the '380 Patent makes the explicit promise that the four compounds identified in claim 1 are “highly useful as anti-hypercholesteremic agents for the treatment of atherosclerosis, hyperlipemia and like diseases in humans”.

[123] The “promise” of the '380 Patent appears to be clearly set out in at least two places in the specification. In the “Summary of the Invention”, at p. 2 of the patent, the patentees state that:

> These new compounds have excellent properties of inhibiting cholesterol biosynthesis and are useful against hypercholesteremia and hyperlipemia.

[124] A slightly more detailed promise is found at p. 3, where the patentees explain that:

> The compounds of this invention are highly useful as antihypercholesteremic agents for the treatment of atherosclerosis, hyperlipemia and like diseases in humans.

[125] Dr. Samson’s opinion is that the detailed statement in the patent (p.3) expresses the promise of the '380 Patent (Samson Expert Report, Exhibit 110, para. 25). Although Dr. Lasure did not directly respond to the question of what was the promise of the patent, she described the uses of the '380 Patent to include the following (Lasure Expert Report, Exhibit 48, para. 21):

> With respect to uses, the ‘380 Patent discloses that the four compounds (and salts and esters of them) can be used to inhibit cholesterol biosynthesis, can be used against hypercholesteremia (high levels of cholesterol in the blood) and hyperlipidemia (high levels of lipids in the blood) and can be used as antifungal agents (to kill or inhibit growth of fungi on plants).

Anti-fungal properties have not been referred to by Apotex in this matter. The issue for this trial is focused on the medical use.

[126] Based on the words of the specification and supported by the opinions of Drs. Lasure and Samson, I find that the skilled person would read the '380 Patent as promising that the compounds (or secondary metabolites) produced from strains of *Aspergillus terreus*, by the fermentation process identified in the patent, are “useful as antihypercholesteremic agents for the treatment of atherosclerosis, hyperlipemia and like diseases in humans”.

I. *Summary on Claims Construction*

[127] Considering the words of the claims of the '380 Patent and the specification and guided by the expert testimony, the relevant claims of the patent should be construed in the following manner:

- Claim 1 is a claim to a process for producing the four identified compounds by a fermentation process using the range of nutrient media and conditions described in the specification (or as would be generally known to the skilled person), following which the compounds are isolated or extracted from the fermentation broth by any of

the known means identified in the specification (or as would be generally known to the skilled person). Of particular relevance to this litigation:

- the micro-organism or fungus to be used is a strain of the species *Aspergillus terreus*, excluding those strains that are unable to produce the desired compounds and excluding micro-organisms from other species within the genus *Aspergillus*; and

- after the fermentation stages of the process, the resulting broth may contain any or all of the four compounds.

[128] With this construction of claim 1, the construction of claims 2 to 8 follows. Each of these claims is a “subset” of claim 1, whereby the claim is restricted to:

- the process of producing only Compounds I and II (claim 2) or Compounds III and IV (claim 5);

- the process of producing the identified compounds using a particular originating micro-organism (claim 3 and 6); and

- the process of producing the identified compounds using certain operational requirements (claims 4, 7 and 8).

[129] Claim 13 claims any one of the four identified compounds (the same compounds as described in claim 1) when made by the process of claim 1 “or by an obvious chemical equivalent”. Claim 14 is a similar claim to either Compound I or II when made by the process of claim 2 “or by an obvious chemical equivalent”. Claim 15 claims each of Compound III and IV when made by the process of claim 5 “or by an obvious chemical equivalent”.

[130] Finally, I find that the skilled person would read the '380 Patent as promising that the compounds (or secondary metabolites) produced from strains of *Aspergillus terreus*, by the fermentation process identified in the patent, are “useful as antihypercholesteremic agents for the treatment of atherosclerosis, hyperlipemia and like diseases in humans”.

VI. Infringement – Background

A. *Introduction*

[131] Having established the proper construction of the relevant claims of the '380 Patent, I now turn to the question of infringement.

[132] Section 44 of the *Patent Act* confers on a patentee and his legal representatives "the exclusive right, privilege and liberty of making, constructing, using and vending to others to be used the invention" of a patent. Merck claims that the Defendants infringed their rights under the '380

Patent by the production of lovastatin using the *Aspergillus terreus* micro-organism. Specifically, Merck claims infringement in three different scenarios:

1. infringement through the manufacture (during Phase 1 of production described above), by AFI in Winnipeg, of quantities of lovastatin included in batch CR0157;

2. infringement, between April 1997 and March 1998, through the manufacture by Blue Treasure of quantities of infringing lovastatin that were shipped to AFI, when Blue Treasure was allegedly "salting" the lovastatin shipments with infringing *Aspergillus terreus* lovastatin; and

3. infringement from March 1998, when Blue Treasure was allegedly shipping lovastatin manufactured with *Aspergillus terreus*.

[133] Subject to the possible exceptions of regulatory or experimental use, the making, constructing, using or vending lovastatin using *Aspergillus terreus* would be an infringement of the '380 Patent. Thus, if Merck can satisfy the Court that certain volumes of lovastatin made from the product received from Blue Treasure were manufactured from or contained, through "salting", *Aspergillus terreus* lovastatin, infringement has been established. Similarly, if Merck can persuade the Court that batch CR0157 contained lovastatin manufactured from *Aspergillus terreus*, infringement has been proved.

B. *Burden*

[134] The first point to be made is that proof of infringement is subject to the civil standard of proof. Merck's burden – whatever it may be – is met if infringement can be shown on a balance of probabilities. Stated in different words, Merck will succeed if it is more likely than not that infringement occurred.

[135] It is trite law that the party alleging infringement bears the burden of proving infringement (see *Monsanto Canada Inc. v. Schmeiser*, 2004 SCC 34, [2004] 1 S.C.R. 902 at para. 29 [*Monsanto*]). However, consideration must be given to the scheme of the *Patent Act* and, in particular, to s. 39(2). Under the *Patent Act* applicable to this action, s. 39(1) provides that:

39. **Naturally occurring substances intended for food or medicine—**(1) In the case of inventions relating to naturally occurring substances prepared or produced by, or significantly derived from, microbiological processes and intended for food or medicine, the specification shall not include claims for the resulting food or medicine itself, except when prepared or produced by or significantly derived from the methods or processes of manufacture particularly described and claimed. [1987, c. 41, s. 14]	39. **Procédés Microbiologiques Naturels—** **(**1) Lorsqu'il s'agit d'inventions couvrant des substances que l'on trouve dans la nature, préparées ou produites, totalement ou pour une part notable, selon des procédés microbiologiques et destinées à l'alimentation ou à la médication, aucune revendication pour l'aliment ou le médicament ne doit être faite dans le mémoire descriptif, sauf pour celui ainsi préparé ou produit selon les modes du procédé de fabrication décrits en détail et revendiqués. [1987, ch. 41, art. 14]

[136] This provision is followed by s. 39(2) which states that:

(2) In an action for infringement of a patent where the invention relates to the production of a new substance, any substance of the same chemical composition and constitution shall, in the absence of proof to the contrary, be deemed to have been produced by the patented process.	(2) Dans une action en contrefaçon de brevet où l'invention porte sur la production d'une substance nouvelle, toute substance formée des mêmes composants et éléments chimiques est, en l'absence de preuve contraire, réputée avoir été produite par la procédé breveté.

[137] On its face, s. 39(2) applies to the facts before me. In Merck's opinion, the '380 Patent is to an invention that relates to the production of lovastatin – a "new substance". The lovastatin produced in any of Phases 1, 2 or 3 of the Defendants' manufacturing is a substance with the same chemical composition and constitution as that produced by the process of the '380 Patent. As such, s. 39(2) would apply and, absent proof to the contrary, such lovastatin would be deemed to be produced by the process of the '380 Patent. With respect to lovastatin manufactured as part of Phase 1 (except for batch CR0157), Merck accepts that there is "proof to the contrary". However, Merck asserts that, for lovastatin that is contained in batch CR0157 and all production sourced from Blue Treasure, s. 39(2) applies and the production must be deemed to be made from *Aspergillus terreus*, thereby infringing the '380 Patent.

[138] The dispute between the parties centres on the meaning of the words "new substance" in s. 39(2).

[139] Merck argues that the substances (Compounds I-IV) claimed in the '380 Patent are new and novel and s. 39(2) is engaged. While there is no definition of "new", the word appears in s. 2

under the definition of “invention”. As such, for patent purposes, “new” could mean novelty, or a product that has not been anticipated.

[140] Apotex submits that the definition of newness has to be determined in light of patent legislation as a whole. Where a word has a meaning in one section, it ought to be the same in every section within a document, absent legislative intent to show that the word can have various meanings. In line with this argument, Apotex’s counsel, in final argument, acknowledged that ss. 2 and 39(2) use the word “new”. However, the word does not appear in provisions that deal specifically with novelty (anticipation): ss. 61, 27, 43. Thus, one cannot say that “new” equates with “anticipation”.

[141] According to Apotex, the interpretation of “new” must fit into the context of s. 39(2) and its commonsense purpose. In oral submissions, Apotex argued that the purpose of s. 39(2) (and its presumption of infringement) was:

> […] to deal with the impossibility of a plaintiff, when it comes to a process in a product-by-process claiming form, not being able, absent proof from the defendant of what that process is, to challenge the infringing nature of that process.

[142] In line with this purpose, once another process is disclosed for the same product, the “newness” of the substance *per se* no longer exists. Apotex also asserted that newness can be lost in a number of other ways: prior commercialization, disclosure and use of the substance.

[143] On the facts of this case, Apotex notes that the application that resulted in Canadian Patent No. 1,129,794 (the '794 Patent or the Endo Patent) related to the claims for lovastatin and

was filed in Canada before the '380 Patent. The '794 Patent also had an earlier priority and issue date. It publicly describes an alternate process to create lovastatin. In Apotex's view, the same can be said for lovastatin created from Red Yeast Rice.

[144] As argued by the parties, there is no direct case law on the interpretation of "new" in s. 39(2). It is helpful to return to first principles of statutory interpretation.

[145] The starting point of my analysis is the general principle clearly stated by the Supreme Court in *Rizzo & Rizzo Shoes Ltd., Re*, [1998] 1 S.C.R. 27 at paragraph 21, 154 D.L.R. (4th) 193 (See also *Bell ExpressVu Ltd. Partnership v. Rex*, 2002 SCC 42, 2 S.C.R. 559 at para. 26, and cases cited therein):

> […] Elmer Driedger in Construction of Statutes (2nd ed. 1983) best encapsulates the approach upon which I prefer to rely. He recognizes that statutory interpretation cannot be founded on the wording of the legislation alone. At p. 87 he states:
>
> > Today there is only one principle or approach, namely, the words of an Act are to be read in their entire context and in their grammatical and ordinary sense harmoniously with the scheme of the Act, the object of the Act, and the intention of Parliament.

[146] *Sullivan on the Construction of Statutes*, 5th ed. (Markham, Ont.: LexisNexis, 2008) (*Sullivan*) comments on the modern principles as articulated by Driedger (p. 3):

> The court must adopt an interpretation that is appropriate. An appropriate interpretation is one that can be justified in terms of (a) its plausibility, that is, its compliance with the legislative text; (b) its efficacy, that is, its promotion of legislative intent; and (c) its acceptability, that is, the outcome complies with accepted legal norms; it is reasonable and just.

[147] Furthermore, in relation to the textual analysis of legislation, there are a number of relevant principles: (a) the presumption of consistent expression (*Sullivan*, above, pp. 214-23), and (b) the presumption of coherence (*Sullivan*, above, pp. 223-25).

[148] Under the principle of consistent expression, it is presumed that the legislature uses language carefully and consistently within the same statute. As such, same words presumptively have the same meanings. On the flip side, one can infer, from the use of different words or a different form of expression, that a different meaning was intended by drafters. This principle was highlighted by the Federal Court of Appeal in *Peach Hill Management Ltd. v. Her Majesty the Queen* (2000), 257 N.R. 193 at paragraph 12, G.S.T.C. 45: “When an Act uses different words in relation to the same subject such a choice by Parliament must be considered intentional and indicative of a change in meaning or a different meaning.”

[149] According to *Sullivan* (pp. 221-22), the strength of this presumption varies. Highly technical statutes and terms that play a key role in the legislative scheme are strongly presumed to have the same meaning throughout. For example the definition of “income” in taxation legislation was considered to be a key term in *Mattabi Mines Ltd. v. Ontario (Minister of Revenue)*, [1988] 2 S.C.R. 175, 53 D.L.R. (4th) 656. The presumption of consistent expression is also strong when the repeated words contribute to a noticeable pattern.

[150] This presumption, however, can be weakened when one examines the context surrounding the words: “Identical words may not have identical meanings once they are placed in different contexts and used for different purposes. This is particularly true of general or

abstract words" (see *Sullivan*, p. 222; *Jevco Insurance Co. v. Pilot Insurance Co.* (2000), 49 O.R. (3d) 760, O.J. No. 2259 (QL) (Ont. Sup. Ct.)).

[151] The other relevant principle is the presumption of coherence. Here, one presumes that provisions of the same legislation are meant to work together logically as parts of a functioning whole.

> The parts are presumed to fit together logically to form a rational, internally consistent framework; and because the framework has a purpose, the parts are also presumed to work together dynamically, each contributing something toward accomplishing the intended goal. […] It is presumed that the body of legislation enacted by a legislature does not contain contradictions or inconsistencies, that each provision is capable of operating without coming into conflict with any other (*Sullivan*, above, p. 223).

[152] In applying these principles, the question is: does "new" in s. 39(2) mean "new" in the ordinary sense, or in the sense of novelty? In other words, to displace the application of s. 39(2), does Merck have to prove that the substance of the product-by-process claim in the '380 Patent was novel, or simply that it was not known before?

[153] For the reasons that follow, I interpret the word "new" to simply mean a substance that was not previously known or used, rather than novelty.

[154] First, within the context of ss. 2 and 39(2), "new" has been used as an adjective. According to the *Gage Canadian Dictionary* (W.S. Avis et al. (ed) (1983), Gage Educational Publishing Co., Toronto), at p. 766, "new" is defined as "not existing before". *Black's Law Dictionary* (6th ed.) (St. Paul, Minn.: West Publishing Co, 1990), at p. 1042 describes "new" as follows:

> […] this word may denote novelty, or the condition of being previously unknown or of recent or fresh origin, but ordinarily it is a purely relative term and is employed in contrasting the date, origin, or character of one thing with the corresponding attributes of another thing of the same kind or class.
>
> In order to be "new", as the word is used in the patent laws, the achievement must be either one that produces an unusual or improved or advanced result, which was unknown to the same prior art at the time of the claimed invention; or the achievement must be one that produced an old result in an unusual and substantially more efficient, or economical way. [Emphasis added.]

[155] As seen above, the ordinary meaning of "new" can equate to novelty or simply a condition of being previously unknown. It is a word that is "purely relative" in nature.

[156] Second, I turn to the contextual meaning of the word "new" within the *Patent Act*. While there is no dispute that patent legislation is highly technical, does the word "new" carry a specific and technical meaning? Is it used in a way that creates a noticeable pattern? Is there a presumption of consistency? My answer to these questions is "no".

[157] "New" in ss. 2 and 39(2) is relative as well; in both instances, the word is used as an adjective to describe different things. Under s. 2, "new" describes how an "art" or

"improvement" can rise to the level of an invention. The notion of novelty is part and parcel of this interpretation.

[158] On the other hand, in s. 39(2), legislators are not describing what constitutes an invention. This provision relates solely to infringement and novelty is not directly at issue. Further, the word "new" is not employed to determine if an "art" or "improvement" constitutes an invention. It merely describes a "substance" or a "product" in a product-by-process claim. There is no requirement that the "substance" be inventive. Section 39(2) deals with the claims in a product-by-process patent. In such claims, the substance cannot be divorced from its process (see s. 39(1) of the *Patent Act*). Accordingly, in a product-by-process claim, whether the substance is novel is not determinative. It is the process of producing the substance that must be novel, new, and inventive. In the context of a product-by-process claim, "new" does not necessitate a novel (not-anticipated) substance.

[159] Third, this interpretation is consistent with the rest of the legislative scheme and avoids internal inconsistencies. If "new" described a novel substance or medicine as the invention *per se*, it would contradict s. 39(1) of the *Act*.

[160] Applying this to the case at hand, the claimed invention is not lovastatin, but lovastatin created through the process of fermenting the organism *Aspergillus terreus*. It is clear from s. 39(1) of the *Act* that the patentee cannot merely claim lovastatin, a medicinal substance, as the invention. Lovastatin is merely the product of the product-by-process claim in the '380 Patent.

[161] Fourth, ss. 27, 43, and 61, which relate to questions of novelty, have no mention of the word new.

[162] Fifth, the jurisprudence supports the interpretation of “new” which means not previously known. According to Justice Nadon, in *Eli Lilly and Co. v. Nu-Pharm Inc.*(1994), 54 C.P.R. (3d) 145 at para. 32, [1994] F.C.J. No. 225 (QL) (F.C.T.D.)[*Eli Lilly and Co. v. Nu-Pharm Inc*. cited to C.P.R.], the presumption of infringement does not arise until the plaintiff has satisfied a minimum evidentiary burden that the substances in question are “new substances”. This means that the initial burden is on Merck to show that the substances created from the process in the ‘380 Patent are “new substances”. The burden is not on Apotex to show that the substances are not new or are anticipated. Since the burden is on Merck to show that the substances created from the process in the ‘380 Patent are “new substances”, to equate “new” with the test of “novelty” would lead to an illogical result. Under the scheme of Canadian patent law, defendants to an infringement action have the burden to prove anticipation (a subset of invalidity). Thus, to have the patentee prove novelty under s. 39(2) would contradict fundamental principles of patent law.

[163] In sum, “new” is a highly relative term and its definition is dependent on its context. Within the context of s. 39(2) of the *Act*, “new substance” means a substance that was not previously known.

[164] With respect to the '380 Patent, the question is whether Compounds I-IV were previously known, or are they simply “old” products? In other words, even if anticipation is not established

by the lovastatin produced by Red Yeast Rice or by the Endo Patent, can lovastatin be said to have been sufficiently “known”, and thus, successfully undermine the “newness” of the substance in the '380 Patent? The answer to these questions is found in the claims construction.

[165] Claim 1 of the '380 Patent clearly states that it is “a process of producing the compounds of the structural formulae [Compounds I-IV]”. While the parties acknowledge that Compound I, lovastatin, is identical to the structure in Dr. Endo’s ‘794 Patent, claim 1 does not solely fence out Compound I, but also II, III, and IV. The Defendants presented no evidence that Dr. Endo knew of, or used, Compounds II, III, and IV. Further, there is no evidence that lovastatin produced by Red Yeast Rice contains Compounds II, III and IV.

[166] Accordingly, I agree with Merck’s argument that the combination of substances produced (Compounds I-IV) is new. There is no evidence that either the Endo Patent or the fermentation of traditional Red Yeast Rice would produce such a combination.

[167] In light of the above, I conclude that s. 39(2) is engaged.

[168] The question that follows is this: If s. 39(2) applies, what is the interpretation of “in the absence of proof to the contrary”? Does it mean that Apotex has an evidentiary burden and that, once this burden is met, the persuasive burden returns to the Plaintiffs to establish infringement? Or does it mean that the persuasive burden is established and therefore Apotex must disprove infringement?

[169] Merck argues that s. 39(2) mandates that the persuasive burden of proof remains with Apotex to show non-infringement. This is supported by the language in the provision – infringement is deemed "in the absence of proof to the contrary". According to Merck, this is different from the presumption of validity, which is weakly worded as merely "in the absence of evidence to the contrary". Merck relies on *Apotex Inc. v. Tanabe* (1994), 59 C.P.R. (3d) 38 at paragraph 92, [1994] O.J. No. 2613 (QL) (Ont. Gen. Div.) [*Apotex v. Tanabe* cited to C.P.R.] to interpret the language in s. 39(2) as creating an onus that it "is not simply an obligation to adduce some evidence to the contrary". Rather, "proof to the contrary" is a "much higher onus than the onus simply to adduce some evidence to the contrary" (*Apotex v. Tanabe*, above, at para. 92). Thus, Merck concludes that s. 39(2) is a provision that deems, rather than presumes, infringement. Consequently, in Merck's view, the persuasive burden is on Apotex to prove non-infringement. I disagree.

[170] Section 39(2) of the *Act* creates a presumption of infringement that confers on Apotex an evidentiary burden to rebut infringement. There is no support for Merck's argument that s. 39(2) deems infringement and puts the persuasive burden on Apotex.

[171] *Hughes & Woodley on Patents*, 2nd ed., looseleaf (Markham, ON: LexisNexis Canada, 2005) at paragraph 45 states that s. 39(2) creates a presumption of infringement:

> This provision creates a presumption of infringement, but, only once an applicant has satisfied a minimum evidentiary burden, establishing that the substances in question are "new" and identical. These provisions, however, may permit the Court to give a broader interpretation of the claims than a mere purposive construction. This is to be contrasted with section 45 of the Patent Act which provides for a presumption of validity in the absence of "evidence" to the contrary. Speculation, as to alternative processes

> that may have been used to produce the product, falls short of the required evidence to the contrary. [Emphasis added; see also *Eli Lilly and Co. v. Nu-Pharm Inc.*, above.]

[172] The text notes that, compared to the validity presumption (rebuttable on an evidentiary basis), the presumption of infringement is stronger. This can be supported by Justice Campbell's decision in *Apotex v. Tanabe* (above, at para. 92). While Justice Campbell held that "proof to the contrary" necessitates a higher standard than "evidence to the contrary", he does not go so far as to say that "proof to the contrary" equates to a persuasive burden to prove a fact on a balance of probabilities. As such, comparing the presumptions of validity and infringement, there is only a difference in degree rather than nature of the burden.

[173] Justice Gibson, in *Abbott Laboratories v. Canada (Minister of Health)*, 2004 FC 1349, 260 F.T.R. 276 at para. 101 [*Abbott Laboratories*], examined the words "in the absence of proof to the contrary" in s. 6(6) of the *Regulations*:

> (6) For the purposes of an application referred to in subsection (1), if a second person has made an allegation under subparagraph 5(1)(*b*)(iv) or (2)(*b*)(iv) in respect of a patent and the patent was granted for the medicinal ingredient when prepared or produced by the methods or processes of manufacture particularly described and claimed in the patent, or by their obvious chemical equivalents, it shall be considered that the drug proposed to be produced by the second person is, in the absence of proof to the contrary, prepared or produced by those methods or processes. [Emphasis added.]

[174] According to Justice Gibson, this provision deals with product-by-process claims, and also creates a presumption that the patent will be infringed. Despite the strong words of "in the absence of proof to the contrary", Justice Gibson was clear that there is no shift in the persuasive burden (*Abbott Laboratories*, above, above, at para. 101).

[175] The Supreme Court, in *Circle Film Enterprises Inc. v. Canadian Broadcasting Corp.*, [1959] S.C.R. 602 at p.604, 31 C.P.R. 57 [*Circle Film* cited to S.C.R], considered similar words in s. 20(3)(b) of the *Copyright Act*, R.S.C. 1927, c. 532: "The author of the work shall, unless the contrary is proved, be presumed to be the owner of the copyright." In seeking to characterize the words in s. 20(3)(b), Justice Judson stated (*Circle Film*, above, at p. 606):

> I take the operation of a presumption of this kind to be as stated by Wigmore on Evidence, 3rd ed., s. 2491(2):
>
> > It must be kept in mind that the peculiar effect of a presumption "of law" (that is, the real presumption) is merely to invoke a rule of law compelling the jury to reach the conclusion in the absence of evidence to the contrary from the opponent. If the opponent does offer evidence to the contrary (sufficient to satisfy the judge's requirement of some evidence), the presumption disappears as a rule of law, and the case is in the jury's hands free from any rule. [Emphasis added.]

[176] In sum, I conclude that the phrase "in the absence of proof to the contrary", in s. 39(2), amounts to an evidentiary burden to rebut the presumption of infringement.

[177] Following this, a number of questions are raised: what is an evidentiary burden? Also, what do the Defendants in this case have to prove in order to meet their evidentiary burden and rebut the presumption of infringement?

[178] On the definition of evidentiary burden, the Federal Court of Appeal in *Hoffmann-La Roche Ltd. v. Canada (Minister of Health and Welfare)* (1996), 70 C.P.R. (3d) 206 at para. 8, 205 N.R. 331 [*Hoffmann-La Roche* cited to C.P.R.] stated:

> […] the "persuasive burden" or the "legal burden", is the burden of establishing a case to the civil standard of proof. By contrast, the "evidential burden" consists of the burden of putting an issue in play and means that a party has the responsibility to ensure that there is sufficient evidence of the existence or non-existence of a fact or an issue on the record to pass the threshold for that particular fact or issue. Nu-Pharm, supra, per Stone J.A., at page 33. [Emphasis added.]

[179] According to the Supreme Court of Canada in *R. v. Fontaine*, 2004 SCC 27, [2004] 1 S.C.R. 702 at paragraph 11 [*Fontaine*], the “evidentiary burden” is not a burden of proof. It is a legal question left for the judge to determine whether “there is some evidence upon which a properly instructed jury could reasonably decide the issue” (*Fontaine*, above, at para. 13). In making such a determination, “the judge does not evaluate the quality, weight or reliability of the evidence” (*Fontaine*, above, at para. 12).

[180] Justice Wetston in *Pharmacia Inc. v. Canada (Minister of National Health and Welfare)*(1995), 60 C.P.R. (3d) 328 at paragraph 28, 92 F.T.R. 253 (F.C.T.D.) [*Pharmacia* cited to C.P.R.], held that the presumption of infringement is bolstered by the common law presumption. According to *Pharmacia*, the common law presumption is (above, at para. 20):

> […] where the subject-matter of an allegation lies particularly within the knowledge of one of the parties, that party must prove it. In this instance, the applicants submit that only the respondent knows the precise composition and process to be used in making their product.

[181] The Court of Appeal in *Hoffmann-La Roche* set out the test for establishing the common law presumption: (a) the defendant asserted no facts to support allegations of non-infringement; (b) the evidence of non-infringement lay peculiarly within the knowledge of the defendant; and (c) the plaintiff had no other available means to access such evidence (above, at para. 8).

[182] Combining principles of the evidentiary burden, the common law presumption and s. 39(2), I conclude that Apotex's burden is to show that it used a non-infringing process to create lovastatin, and that this process was disclosed to Merck. At this time, the Court should not assess the quality, weight or reliability of the evidence, but merely ask if there is sufficient evidence to put the issue in play.

[183] I find that Apotex, by its disclosure of the AFI-4 process (fermenting *Coniothyrium fuckelii* to produce lovastatin), has met its evidentiary burden to rebut the presumption of s. 39(2). Merck has accepted that the non-infringing AFI-4 process was used at the AFI plant in Winnipeg to produce lovastatin (except for CR0157). Because Apotex has met its evidentiary burden, the presumption of infringement has been rebutted. In the words of Wigmore, "… the presumption disappears as a rule of law and the case is in the jury's hands free from any rule" (*Circle Film*, above, at p. 606). The persuasive burden of proof is back with Merck.

[184] By way of summary, the burden within s. 39(2) of the *Act* is as follows:

a) Merck has the evidentiary burden to prove its substance is "new" in order to engage s. 39(2);

b) Apotex then has the evidentiary burden to prove a viable alternative process existed to create lovastatin that does not infringe the '380 Patent – if this is done, the presumption of law is lifted; and finally,

c) Merck has the persuasive burden to prove infringement.

[185] On the facts of this case, I am persuaded that the '380 Patent involves a “new substance” thereby engaging s. 39(2). Apotex has established that a viable alternative exists that does not infringe the '380 Patent. Accordingly, Merck has the persuasive burden to satisfy me, on a balance of probabilities, that Apotex’s sale of lovastatin, manufactured by Blue Treasure lovastatin or out of batch CR0157, was made by a process that infringed the '380 Patent.

[186] I turn now to consider whether Merck has met its burden. In my view they have, with respect to some of the lovastatin manufactured by Blue Treasure and lovastatin that originated from AFI batch CR0157.

C. *Summary of Merck’s case on infringement*

[187] As noted above, Merck claims infringement of the '380 Patent in three different scenarios:

1. infringement, between April 1997 and March 1998, through the manufacture by Blue Treasure of quantities of infringing lovastatin that were shipped to AFI,

when Blue Treasure was allegedly "salting" the lovastatin shipments with infringing *Aspergillus terreus* lovastatin;

2. infringement from March 1998, when Blue Treasure was allegedly shipping lovastatin manufactured with *Aspergillus terreus*; and

3. infringement through the manufacture (during Phase 1 of production described above), by AFI in Winnipeg, of quantities of lovastatin included in batch CR0157.

[188] I will deal with each of these scenarios separately.

VII. Infringement – the Circumstantial Case

A. *Blue Treasure "Salting"*

[189] Merck asserts that Blue Treasure was "salting" its earlier shipments of lovastatin with infringing AFI-1 lovastatin. In simple terms, Merck submits that Blue Treasure was "diluting" its AFI-4 lovastatin with AFI-1 lovastatin, thereby infringing the '380 Patent with each and every shipment of lovastatin to AFI.

[190] On March 18, 2010, Merck received a copy of an e-mail, dated September 8, 1997 purportedly from Dr. Su to his "managers" at AFI. In the e-mail, Dr. Su wrote that "before the switchover, [Blue Treasure] . . . produced 296.6 kg #1 product". This 296.6 kg product is the

basis of Merck's salting argument. The Defendants have not provided evidence as to how this quantity of AFI-1 lovastatin was sold or disposed of.

[191] Does the failure of Blue Treasure to account for this quantity of AFI-1 lovastatin lead to a finding, on a balance of probabilities, that this lovastatin ended up being shipped to Canada as a "salted" mixture with non-infringing AFI-4?

[192] Merck argues that, absent evidence of the whereabouts of the entire 296.6 kg, the reasonable inference is that all or part of that quantity of AFI-1 lovastatin was used to "salt" the AFI-4 lovastatin. By salting the Winnipeg shipments with infringing lovastatin, Merck asserts that Blue Treasure was able to sell the more cheaply-made lovastatin where payment was priced, on a kilogram basis, on the more costly AFI-4 lovastatin. Blue Treasure was also thereby able to dispose of its aging inventory of infringing lovastatin that could not be moved on the domestic Chinese market. According to Merck, if there were an innocent explanation for Blue Treasure's disposition of the infringing lovastatin, AFI would have provided it; none has come.

[193] In addition to the Defendants' failure to provide sufficient information on the disposal of 296.6 kg of AFI-1 lovastatin, Merck points to two other key factors which, in their view, support the allegation of "salting". The first point is the evidence that demonstrates the difficulty that Blue Treasure was having selling lovastatin into the Chinese or other foreign markets at a reasonable profit. (This evidence is discussed at some length in the section of these reasons dealing with "motivation".)

[194] Moreover, Merck refers to AFI's concern that unusually low levels of RC-14 were found in the first two shipments of lovastatin from Blue Treasure. Merck argues that AFI had been worried enough about the possibility of "adulteration" that Dr. Su was sent to Blue Treasure to investigate and supervise the Blue Treasure lovastatin productions. No determination was ever made by Dr. Su about the reason for the unusually low levels of RC-14 in the shipments of AFI-4 lovastatin. Merck appears to argue that the RC-14 level could be explained if the shipment to AFI had been, in fact, a mixture of AFI-1 and AFI-4 lovastatin.

[195] In a letter dated August 11, 1997, Dr. Cox advised Mr. Zhou that:

> I was very disappointed to learn that 2 out of 3 batches of lovastatin made by the new AFI process had failed our quality control, partly because your people had unilaterally made changes to our process.

[196] The most worrying problem with the lovastatin batches was the low levels of a compound known as RC-14. In a letter from Mr. Alexander (Sandy) Fowler (Finance Manager at AFI) to Mr. Zhou dated September 12, 1997, Mr. Fowler described the "puzzle" as follows:

> Our scientists are very concerned in regard to the low levels of RC14 in certain of the batches produced at Blue Treasure. At [AFI], we have never produced AFI-4 lovastatin with such low RC14. In fact, in our experience, the "signature" of AFI-4 is a higher level of RC14.

[197] Low levels of RC-14 were characteristic of AFI-1. Thus, it is clear that the real concern was whether the AFI-4 lovastatin was being produced using AFI-1 or was being contaminated in some way by the *Aspergillus terreus* strain. During his oral testimony, Dr. Cox was very direct in his testimony about the lack of trust between AFI and Blue Treasure. The decision was made by

AFI to send Dr. Jerry Su to Blue Treasure to work with the management team (see letter dated August 18, 1997 from Dr. Cox to Mr. Zhou).

[198] Dr. Jerry Su was the Group Leader of Research & Development at AFI from September 1996 to December 1998. Dr. Su arrived in China on August 28, 1997 and remained there until the end of October 1997. As set out in his "Report on the work at Blue Treasure", dated November 13, 1997, his primary task was to ensure that Blue Treasure maintained all fermentation free of contamination from the *Aspergillus terreus* strain. He investigated the low levels of RC-14 but, even after his time in China and his examination of a number of possible reasons, the cause of low RC-14 levels in two batches was still a "puzzle". Nevertheless, Dr. Su appeared to be satisfied that the runs conducted while he was at Blue Treasure would meet the quality control standards at AFI.

[199] Together, Merck submits, all of this evidence is consistent with a finding that, on a balance of probabilities, Blue Treasure was mixing infringing AFI-1 lovastatin with the AFI-4 lovastatin that was being shipped to AFI from Blue Treasure.

[200] In terms of the technical feasibility of salting, Merck relies on the statement of Dr. Cox who testified that there is nothing difficult about salting:

> Q. You understood, at the time, doctor, that Lovastatin made from one process could be made and mixed with Lovastatin made using another process; you understood that was a technical feasibility?
>
> A. It's very straightforward. You put them together and mix them.

[201] I agree with Merck that the Defendants – in particular AFI – have presented obstacles to uncovering relevant facts related to the amount of AFI-1 lovastatin actually produced and sold by Blue Treasure. Once the e-mail of Dr. Su came to light on March 18, 2010, Merck sought and was granted, on consent, an opportunity for further discovery of Mr. Fowler. Mr. Fowler has been the Finance and Administration Manager at AFI since 1996. Questions related to this lovastatin were put to Mr. Fowler and taken under advisement by counsel for AFI. AFI refused to provide confirmation of the 296.6 kg quantity (Undertaking #2319). In Undertaking #2320, AFI was also asked, in respect of the 296.6 kg product:

> To advise full particulars, when it was made, what happened to it, who it was sold to, for how much and financial benefits to AFI and Apotex.

[202] All of this information was refused. Although Apotex refers to some evidence on the record that directionally supports legitimate sales of AFI-1 lovastatin, the information is far from complete or clear.

[203] In spite of my serious concerns about the unwillingness or inability of the Defendants to provide evidence concerning the alleged 296.6 kg product, I have problems with Merck's argument on this point.

[204] My first concern is that I have little evidence that Blue Treasure produced 296.6 kg of AFI-1 lovastatin. In Dr. Su's e-mail, there is the reference that, "before the switchover, [Blue Treasure] . . . produced 296.6 kg #1 product". There is no indication in the e-mail of where this number came from. Contrary to the assertion by Merck, the e-mail does not "prove" the existence of 296.6 kg of infringing lovastatin.

[205] The second problem is that I have no evidence, beyond the cryptic statement of Dr. Cox, as to how salting could be carried out. No expert spoke to the practice. As noted by counsel for Apotex in final argument:

> . . . there was no evidence led as to how you put together AFI-1 material with AFI-4 material, whether the appearance and composition of technical grade lovastatin, colour wise, physical characteristics, crystallinity, whether that is comparable.

[206] In addition, I have no confirmation from anyone that low levels of RC-14 could be explained by salting. That question could have been posed to any number of witnesses by Merck and was not. The closest discussion on the record occurred during the cross-examination of Mr. Fowler. Mr. Fowler was questioned at length about why Dr. Su was sent to China. Specifically, the concern that Blue Treasure had switched the organisms was put to Mr. Fowler. His response included a vague reference to the possibility of "contamination or mixing of product":

> The concern from my perspective was that there not be any mix-up or errors resulting in a contamination or mixing of product, that sort of thing. Certainly, in everybody's mind there was a possibility of some mix-up, and that's what we wanted to get to the bottom of.

This statement is certainly not sufficient for me to conclude that AFI believed that "salting" was going on at Blue Treasure.

[207] I conclude that it is possible that Blue Treasure used some of the alleged 296.6 kg of AFI-1 lovastatin to "salt" the AFI-4 lovastatin being shipped to AFI. However, on the evidence before me, I have insufficient evidence about how that could have been done from a technical

perspective. Nor do I have any evidence that AFI believed that “salting” might have been the reason for the low levels of RC-14.

[208] In short, Merck has failed to persuade me, on a balance of probabilities, that any quantities of lovastatin were salted with infringing lovastatin.

B. *Infringement by Blue Treasure from March 1998*

[209] As I understand Merck’s argument on infringement after March 1998, the key reasons why I should find that the lovastatin manufactured by Blue Treasure and sold to AFI for sale in Canada, was produced using a process that infringed the '380 Patent are as follows:

- The Batch Records (referred to below) produced by Blue Treasure to demonstrate the use of the non-infringing AFI-4 process for producing lovastatin are not genuine.

- The Defendants failed to provide evidence that Blue Treasure acquired sufficient quantities of a compound known as P2000 with which to carry out fermentations with the *Coniothyrium fuckelii* micro-organism.

- The reduction in the duration of fermentation, beginning in March 1998, is unexplained except by the use of the infringing process.

- The increase in the quantities of titres, beginning in March 1998, is unexplained except by the use of the infringing process.

- Blue Treasure had the motivation, the means and the opportunity to produce lovastatin with the less expensive, more efficient AFI-1 infringing process.

- The conduct of Blue Treasure before and during this trial is consistent with infringement.

[210] In addition to the above – much of which consists of circumstantial evidence – Merck asserts that it has direct evidence of infringement through the DNA evidence put forward by Dr. Julian Davies.

(1) Batch Records

[211] Standard pharmaceutical industry practice requires that detailed and exact records be kept of all steps in the production of pharmaceutical products. In this trial, the Defendants put forward 364 documents as true photocopies of the batch records for 364 fermentation batches of lovastatin made at Blue Treasure (the Batch Records). There is no doubt that, if the Batch Records (all of which are contained in Exhibit 149) can be believed, they are direct evidence that Blue Treasure was using the non-infringing AFI-4 process and not a process using *Aspergillus terreus*. However, the issue is whether I can believe that the Batch Records are reliable, or even truthful, in some important aspects. Quite simply, I cannot.

[212] The first problem with the Batch Records is that they are not the original working records from the batches. The original Batch Records, together with every single related document and working paper, were destroyed in 2003. All that is before this Court are photocopies of what is alleged to be the original batch records.

[213] The Batch Records were introduced into evidence by Mrs. Quifen Hu. Mrs. Hu has been the Manager of the Bacterial Culture Department at Blue Treasure since 1995. From 1991 to 1994, she was the Manager of the Intermediates Department at New North River in China. Since 1995, Mrs. Hu's responsibilities have mainly related to maintaining the seed bank at Blue Treasure and initializing the fermentation process for the production of lovastatin.

[214] Each of the 364 Batch Records is substantially the same in format; each appears to be a pre-printed form with data and other entries written by hand. They reflect fermentations that began on May 27, 1997, with batch no. CF-403-97001, and ran until the fermentation of batch no. CF-410-99166, which began on September 29, 1999.

[215] Parts 1.1 and 1.2 are entitled "Production Record of Lovastatin Fermentation". The list of ingredients of the medium is printed on the form and the quantities used are hand written in the appropriate space. Information on the pH adjustment and the steps for inoculation of the seed flasks are documented. The final step described is the culture of a second seed flask.

[216] Parts 2 to 14 of each batch record set out the scale-up of fermentation from the final step of Part 1.2 to Part 13, which is entitled the "Production Fermenter", where the final product is

fermented. Along the way, increasingly larger fermenters are prepared and then inoculated with the seed media from the previous stage.

[217] The only place that the initiating or seed micro-organism is described is in Parts 1.1 and 1.2. The batch no. is recorded on the cover sheet of each batch record and on most pages, and always begins with the letters “CF”. Presumably, this means that the particular run is being carried out with *Coniothyrium fuckelii*. In addition, each of the 364 Batch Records is pre-printed with an entry that identifies the production strain as “*Coniothyrium fuckelii* AFI-4 85-42”. For Parts 2 to 14, no strain is identified.

[218] Mrs. Hu was responsible for overseeing the process to the end of Part 1.2. After that, the production steps were within the responsibility of the Fermentation Production Department, where Mr. Dingjun Luo (whose testimony is referred to later in these Reasons) worked.

[219] The first point to make about the Batch Records is that they do not qualify as business records that can be accepted for the truth of their contents as an exception to the hearsay rule of evidence.

[220] Since *Ares v. Venner*, [1970] S.C.R. 608 at p. 363, 12 C.R.N.S. 349, the common law in Canada has recognized that certain records:

> . . . made contemporaneously by someone having personal knowledge of the matters then being recorded and under a duty to make the entry or record should be received in evidence as *prima facie* proof of the facts stated therein.

[221] The common law has been codified in s. 30(1) of the *Canada Evidence Act*, R.S.C. 1985, c. C-5:

Where oral evidence in respect of a matter would be admissible in a legal proceeding, a record made in the usual and ordinary course of business that contains information in respect of that matter is admissible in evidence under this section in the legal proceeding on production of the record.	Lorsqu'une preuve orale concernant une chose serait admissible dans une procédure judiciaire, une pièce établie dans le cours ordinaire des affaires et qui contient des renseignements sur cette chose est, en vertu du présent article, admissible en preuve dans la procédure judiciaire sur production de la pièce

[222] The evidentiary record on the Batch Records is, to put it bluntly, a mess. One thing that I can say with certainty is that the Batch Records reflected in Exhibit 149 were not made contemporaneously with the fermentations to which they ostensibly relate. I need only compare these Batch Records to those produced as part of the production runs at AFI. The AFI records contain numerous corrections and deletions. From the writing styles, it is clear that a number of persons completed the documents at various stages of each fermentation. In contrast, the Batch Records do not contain a single strike-out or correction; they, as described by counsel for Merck, are "pristine". This would be unheard of in any production facility.

[223] As I understand it, AFI acknowledged, late in the trial, that the staff at Blue Treasure completed unilingual Chinese work sheets on the plant floor and that, subsequently, the data collected was transposed into bilingual batch records. Other evidence, provided through an Undertaking, is that Mr. Luo confirmed that unilingual sheets "did exist and that information from those sheets . . . were transferred into the bilingual batch record".

[224] If these are not business records, the question becomes: how much, if any, weight should be given to the Batch Records?

[225] Three witnesses provided testimony on the Batch Records – Mr. Dingjun Luo, Mrs. Hu and Dr. Jerry Su.

[226] The best evidence of how the Batch Records were created, and by whom, was provided by Dr. Jerry Su. As noted earlier, from September 1996 to December 1998, Dr. Su was the Group Leader of Research & Development at AFI. He has not worked for AFI since that time. Dr. Su was quite firm in his recollection, having spent long hours at the Blue Treasure plant observing and taking notes as to the daily operations. The following flows from Dr. Su's testimony:

- Blue Treasure maintained two sets of batch records. There were no "unilingual worksheets" for part of the process, only the original Chinese language batch records, which Dr. Su called the "first set" of batch records. These were used on the plant floor and entries were made therein by operators.

- The first set of batch records was collected and the data therein were copied out, by hand, into a "second set" of bilingual batch records.

- Dr. Su sat next to, and witnessed, the person copying the batch records, but did not see whether the information was accurately being copied.

- The person who copied the data into the second set of batch records (apparently the originals of the ones before the Court) was Mr. Luo, Manager of the Production and Technology Department.

- Dr. Su did not recall ever seeing Mrs. Hu signing any of the Batch Records.

[227] I have no reason to disbelieve Dr. Su and, where there is conflicting testimony from Mrs. Hu or Mr. Luo, I prefer the testimony of Dr. Su. At present, Dr. Su has no connection with AFI or Blue Treasure and no motive to fabricate his evidence. His explanation of the transfer of data from the original working documents is logical and consistent with the form of the Batch Records that make up Exhibit 149.

[228] Mr. Luo's testimony was presented by AFI in an attempt to validate the Batch Records as reliable documents. Mr. Luo is currently Deputy General Manager with Blue Treasure. He first joined Blue Treasure, as a technician, in 1995. In 1996, he described his position at Blue Treasure as Head of Production and Technology.

[229] Mr. Luo was a very difficult witness. AFI's counsel admitted, in oral final argument, that there were problems with Mr. Luo's testimony. As the evidentiary record with respect to the Chinese Journal Articles demonstrates (see para. 322 of these reasons), Mr. Luo was prepared to fabricate evidence when it served his purpose. His testimony was replete with poor memory of matters that ought to have been known to him. In spite of his senior position at Blue Treasure, he

claimed to be unaware of any matter that did not fall directly under his supervision. His evidence on the subject of the Batch Records was particularly problematic.

[230] When cross-examined on the question of the second set of Batch Records, Mr. Luo was unequivocal:

> Q. Thank you, sir. Did you tell the lawyers that there was a unilingual Chinese worksheet from which data were copied into a second set of batch records?
>
> A. There is no such first set and second set of records.
>
> Q. Did you tell the lawyers that a unilingual worksheet, containing the parameters mentioned in a letter from February, were prepared and that those data were copied into the second set of batch records which have been produced in the litigation? Did you tell the lawyers that?
>
> A. No.

[231] The problem is that Mr. Luo provided a different and conflicting explanation about the Batch Records, recorded as a response to Undertaking # 6585:

> Mr. Luo advised that it was the operators that transferred information from the unilingual worksheets into the bilingual English/Chinese batch record. He would then check the bilingual batch record to ensure that it was accurate and that no information was missing.

[232] As demonstrated by these examples and other portions of the record, the evidence of Mr. Luo with respect to the Batch Records lacks credibility.

[233] Another witness who spoke about the Batch Records was Mrs. Hu. Apotex submits that I should accept Mrs. Hu as a reliable witness. I find that difficult to do.

[234] Mrs. Hu was an evasive and difficult witness. Her testimony on the Batch Records was no less confusing than that of Mr. Luo. Repeatedly, she refused to acknowledge matters that should have been within her knowledge. She was lead extensively through her direct testimony. In general, her testimony in chief was a reading of the Batch Records. Mrs. Hu's recollection of making lovastatin with *Coniothyrium fuckelii* from May 1997 to October 1999 and her testimony with respect to the Batch Records were not consistent and did not stand up on cross-examination.

[235] When taken to the cover page of the batch record for the first run of AFI-4, Mrs. Hu testified that she signed the original of this batch record on May 26, 1997, the date reflected on the record. Similarly, she testified that she signed each and every one of the 364 Batch Records on the date that the various operations were performed. She vehemently and – in my view – illogically clung to her testimony that she herself signed the record on each and every day. Mrs. Hu also testified that there were no unilingual Chinese records and that she had never seen anyone writing numbers on a separate work sheet for copying into the batch records later. This, of course, is not what the Court was told by Dr. Su. Moreover, her testimony that there were no unilingual or working records is inconsistent with the "pristine" appearance of the Batch Records in Exhibit 149.

[236] Mrs. Hu may well have signed at the appropriate spots in Parts 1.1 and 1.2 of the reconstructed Batch Records. She may well have believed that Parts 1.1 and 1.2 of the Batch Records accurately reflected what she had done at that stage of the fermentation runs. However, I find, as a matter of fact, that she did not do so contemporaneously with the fermentation runs. Rather, she signed the pages after Mr. Luo had completed the forms. It is difficult to say whether

Mrs. Hu, whose testimony demonstrated no understanding of the English language, was even able to read what was printed and written on the forms or took the time to compare the information on the original operational records to the headings and data that appeared in Parts 1.1 and 1.2 of the Batch Records. The original records could have helped corroborate her testimony; sadly, they were destroyed. Most significantly, Mrs. Hu's testimony does not reliably establish which runs, if any, were made using AFI-4, in spite of the use of the identifier "*Coniothyrium fuckelii* AFI-4 85-42" on each of the Batch Records.

[237] In sum, I am not persuaded that the Batch Records contain the original data from the 364 fermentations allegedly carried out by Blue Treasure; rather, they were transcribed from the originals, most likely by Mr. Luo.

[238] Another area of concern regarding the Batch Records was the destruction of the original documents in January 2003. The fact that the original batch records were destroyed six years into this litigation by Blue Treasure, a joint venture in which the Defendants are partners, raises a serious concern. Were they destroyed, as asserted by Merck, to hide evidence of the actual production methods?

[239] Mrs. Hu's testimony on why the original batch records were destroyed was inconsistent and illogical. According to Mrs. Hu, she was the person who authorized the destruction of the originals. She testified that she did so pursuant to a Chinese GMP policy (apparently entitled "Guidance for Industry – Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients"). However, when questioned about the policy, it was clear that she

did not have even the most basic understanding of the policy. Mrs. Hu was unable to recall clearly any of the details related to the destruction. She could not remember clearly the last time she signed a request for destruction. Finally, the copy of the GMP Policy presented to the Court was apparently brought into effect in April 2003 – three months after the alleged destruction. I am left without any reasonable explanation as to why the original records were destroyed.

[240] I find that the original batch records were destroyed for reasons that cannot be determined, thereby leaving me unable to confirm any of the information contained in the Batch Records.

[241] Moreover, any further confirmation of how and when the Batch Records were actually prepared is impossible. Mr. Brian Lindblom, recognized by the Court as an expert in forensic document examination, provided helpful opinions regarding this issue. Mr. Lindblom examined the Batch Records and, in his Expert Report, provided the following list of relevant tests that he would have performed on the original documents had they been available to him (Lindblom Expert Report, Exhibit 66, para. 19):

> (a) whether the paper used in the original batch record was in fact available at the time the documents were allegedly made;
>
> (b) whether all of the inks used in the original batch record were in fact available at the time the documents were allegedly made;
>
> (c) whether the ink has been on the document for the amount of time indicated by the date of the batch record;
>
> (d) whether a single ink had been used for a batch record supposedly completed by numerous people over many days (in which one would expect to find more that one ink type);

(e) whether and perhaps when alterations had been made to documents which might suggest some type of fabrication;

(f) whether the documents were in fact completed in the chronological fashion suggested by the time line set out in the batch records (this can be determined through examination of indentations); and

(g) whether more than one person completed the handwriting on the batch record (as one would expect for a process which occurred over many days).

[242] I conclude that the Batch Records are not reliable or trustworthy evidence that the fermentation runs that took place at Blue Treasure after March1998 were using the AFI-4 process to produce lovastatin. The pre-printed forms could have easily referred to *Coniothyrium fuckelii* as the production strain, even if a strain of *Aspergillus terreus* was used. The data could readily have been changed to cover up the use of the AFI-1 infringing process. Indeed, the lack of credibility of the two Blue Treasure witnesses leads me to conclude that it is more likely than not that the Batch Records were fabricated, at least with respect to any information that could identify the strain of micro-organism used.

[243] The Batch Records and the testimony of Mr. Luo and Mrs. Hu are critical underpinnings of the Defendants' defence to the allegation of infringement. In my view, the Batch Records contain data about the fermentations that are not consistent with that defence.

[244] Apotex asserts that Merck's argument that the Batch Records should not be relied on is inconsistent with Merck's use of the data to highlight the problems with the titres, the use of P2000 and the reduction in fermentation duration. I do not find the position of Merck, when

explained in oral argument, to be inconsistent. I believe that what Merck is saying is that the Batch Records should be completely rejected. In the absence of reliable records on the fermentations, Merck asserts that the Defendants have no defence to the allegation of infringement. However and alternatively, Merck argues, if the Batch Records are to be believed, the data demonstrates that Blue Treasure must have been using the infringing AFI-1 process after March 1998.

[245] On a final note, the Defendants submit that I should exercise caution in assessing the credibility of Mrs. Hu and Mr. Luo. In particular, they point to the existence of cultural differences that could account for the behaviour or demeanour of these witnesses.

[246] This concern about applying “western” standards to an assessment of credibility was considered, in a criminal context, by the Ontario Court of Appeal in the case of *R. v. E.(T).*, 2007 ONCA 891, [2007] O.J. No. 4952 (QL) [*R. v. E.(T).*]. In that case, the trial judge stated that he did not believe the accused, relying heavily on the demeanour of the accused during his testimony. The Court of Appeal at paragraph 5, in finding that the judge erred, stated as follows:

> The appellant contends that the trial judge's references to the appellant's apparent passivity and to his failure to make eye contact with the other witnesses at the trial constitute erroneous use of demeanour evidence. We agree. As the trial judge himself observed, accused persons can react differently in a stressful criminal trial. Without explaining why, and without acknowledging the effect of cultural background on demeanour (the appellant was born and raised in Sudan), the trial judge equated passivity and an absence of eye contact with witnesses with rejection of the appellant's credibility and, ultimately, his testimonial denial of committing the offence. This equation is, in our view, a misconceived and improper linkage.

[247] In the criminal context, there is a significant difference in burden and standard of proof. The Crown, in *R. v. E.(T.)*, bore the burden of proving all of the elements of the alleged offence beyond a reasonable doubt. It was open to the Crown to put forward expert evidence on cultural background; had it done so, the outcome in the Court of Appeal's decision might have differed. Further, it appears, from reading the judgment of the Court of Appeal, that the trial judge placed much of his reliance on the demeanour of the accused; as noted by the Court of Appeal, the trial judge "equated" demeanour with rejection of the accused's credibility.

[248] In the case before me, Mrs. Hu and Mr. Luo are the Defendants' witnesses. They were put forward expressly to respond to the claim by Merck that Blue Treasure was, at least in part, using the infringing AFI-1 process. During their appearances, I was never alerted to the fact that any cultural background issues would alter how they presented themselves. Nor did the Defendants put forward any expert testimony on what these alleged "cultural differences" could be. In fact, beyond a general caution, the Defendants make no attempt to describe what particular attributes would affect the testimony or to describe what specific aspects of their demeanour reflect a cultural difference. In the circumstances, I can see no reason why I should not rely on demeanour (within reason and not solely) in assessing their credibility.

[249] Having said this, however, I am aware that both Mrs. Hu and Mr. Luo testified through an interpreter. Even with competent translation (which we had in this trial), I can appreciate that there may be times where the witnesses could have become frustrated with the inability to testify directly. This frustration was readily apparent with Mrs. Hu – less so with Mr. Luo. In those

situations, the answers may not have been as clear as they could have been. I have taken that into account.

(2) P2000

[250] The evidence before me is that the compound known as Polyglycol P2000 (P2000) was an essential ingredient in the AFI-4 process. As I understand it, foaming created by the fermentation process negatively affects the production levels. When P2000 was added to the fermenters it acted as an anti-foaming agent and increased the titres dramatically. Without P2000, it is fair to say that the production of lovastatin using *Coniothyrium fuckelii* would not be commercially viable.

[251] Dr. Connors, an expert witness who provided the Court with his understanding of the history of the AFI-4 process at AFI, spoke in superlatives about the decision to add P2000 to the process. According to Dr. Connors, the addition of P2000 to the fermentation medium in March 1995 was a key breakthrough in the development of the AFI-4 process at AFI:

> This is March of 1995. This is really the big break in the project. I will take you to, under tab 63, AFI production 4-39, the very first one. This is when you are glad to be a scientist. This is when you are glad that you chose science. This, again, is culture 115 57, and this is the first data that suggests that adding P2000 in larger amounts than what you would normally add it gives you a dramatic increase in the production of Lovastatin with this culture.
>
> You can see through the top row of data that day six, day seven, day eight titers, 300 mgs per litre. If you increase the P2000 up to two percent or 20 mls per litre, by day eight you have almost 1.6 grams per litre. Spectacular. I mean, this is incredible.

> You can see, also, more importantly too, or just as important, that this is a dose dependant manner. As you increase the concentration of P2000 incrementally, you see a concomitant increase in the titer of Lovastatin as well. So this was a very good result. This was something that really broke the project open for them.
>
> [Emphasis added.]

[252] The increased amount of P2000 needed for the AFI-4 process as compared to the AFI-1 process is dramatic – in the order of 10 to 20 times more is required for the AFI-4 process. Mr. Scott Primrose is a senior research scientist at AFI. In 1993, he was working in the microbiology laboratory of AFI, where much of his work focussed on the development of non-infringing lovastatin – that is, the AFI-4 process. He confirmed that the AFI-1 process required about 1/20th of the amount of P2000. Dr. Sailer described the amount of P2000 used for the AFI-4 process as "very unusual":

> Typically amount of anti-foam used for fermentation it's like point two percent and in this case was two percent, 10 times more. [Emphasis added.]

[253] Merck submits that Blue Treasure did not have sufficient quantities of P2000 to complete 364 runs of the AFI-4 process. Merck calculated that Blue Treasure would have needed 73,338 kg of P2000 to run 364 fermentation batches. This calculation was not disputed by the Defendants. Blue Treasure also needed P2000 for other projects, including for the production of compactin and AFI-1 lovastatin.

[254] How much P2000 did Blue Treasure have? According to the evidence, between May 1, 1997 and June 9, 1998, AFI made 10 shipments of P2000 to Blue Treasure for a total of 27,784.80 kg. This would have been far short of the 73,338 kg needed to run the AFI-4 process,

but certainly sufficient to supply the AFI-1 process. Approximately 5 to 10% of the amount of P2000 is needed for the AFI-1 process. How did Blue Treasure obtain the remaining P2000 that it needed? There really was no answer to that question.

[255] Dr. Connors speculated as follows:

> The balance of the P2000 could have come from someplace else. Might have been the amount they started with. Perhaps this was the amount of raw material that Winnipeg provided, and P2000 was sourced through some local vendor. P2000 is not an unusual chemical. It's a commodity, and could very well be available in China. I don't know for sure.

[256] The Defendants assert that, after July 1998, Blue Treasure began to source its own raw materials, including P2000. Mr. Fowler, speaking to this issue during his testimony, stated that "after the fifth order [for P2000] Blue Treasure was able to purchase its own raw materials". However, Mr. Fowler provided nothing beyond speculation that Blue Treasure was accessing P2000 from other markets; he had no personal knowledge of how that might have happened or if, indeed, it did.

[257] Beyond the speculation of Dr. Connors and Mr. Fowler, I have nothing that speaks to Blue Treasure's acquisition of the required quantities of P2000. I have seen no invoices or shipment statements to back up the Defendants' assertions in this regard.

[258] The missing P2000 is extremely important. Without sufficient quantities of P2000, Blue Treasure could not have produced AFI-4 lovastatin throughout the entire 364 runs. There are obviously people associated with Blue Treasure who could have provided evidence of additional

purchases of P2000, if such purchases had taken place. For example, Mr. Zhou was the Plant Manager at the relevant time. Of those who might have been able to assist the Court, only Mr. Luo was called as a witness and he was not asked about P2000. In the circumstances, I will presume that the evidence that could have been provided by the witnesses from Blue Treasure, who were not called to testify, would have adversely affect the Defendants' case (see *Levesque v. Comeau*, [1970] S.C.R. 1010, 16 D.L.R. (3d) 425). In other words, I will assume that Blue Treasure has no further evidence that it ever purchased enough P2000 to carry out the 364 fermentations using the AFI-4 process.

[259] In the absence of evidence to the contrary, it is not unreasonable to believe that Blue Treasure was not using the AFI-4 process as the Defendants claim. On the other hand, I have evidence that the Blue Treasure had sufficient P2000 - 27,784.80 kg – to carry out the fermentations using the AFI-1 infringing process. I have persuasive evidence – albeit circumstantial – that supports a conclusion that Blue Treasure was using the infringing AFI-1 process to produce lovastatin.

(3) Fermentation Duration

[260] One of Merck's arguments focuses on the notion of "fermentation duration". As discussed in the background section of these reasons, the production of lovastatin requires fermentation over a period of time. It is self-evident to say that a manufacturer will try to produce the largest volume of final product over the least amount of time. For example, in

general, producing 100 units of material over 10 days is economically more efficient than producing the same 100 units over 12 days.

[261] Production of lovastatin is reported in “titres” (also “titers”) – that is, the concentration of a solution as determined by titration, usually measured in units of mg/L or g/L.

[262] Dr. Mila Sailer explained “fermentation duration” as the interaction of a number of factors. Dr. Sailer was a fact witness presented to the Court by AFI. Dr. Sailer worked as a natural product chemist with AFI, and was involved in the production of lovastatin in October 1996 when AFI started its first commercial production of lovastatin from *Coniothyrium fuckelii*. Dr. Sailer explained that production of a product such as lovastatin requires consideration of a number of factors:

> There is a number of factor which is to be considered when you, when you want to optimize the production of the facility, fermentation facility. So, for instance, you have to look on the production curve doing the fermentation run, you have to look on a capacity of the seed train which is used for inoculation of production vessels. You have to look on the capacity of the downstream equipment. You have to look on, for instance, on impurity profile during the fermentation run, which can change. You have to look on cost of the media.

[263] Under the notion of the “production curve”, Dr. Sailer spoke about fermentation durations and confirmed that often there is a trade-off between titres and fermentation times. Sometimes, he said “it’s not the best to . . . go for maximum titres”; rather, “sometimes it’s much better to shorten the time and do a higher number of fermentation[s]”. While Dr. Sailer was not presented as an expert, his testimony codifies common sense when it comes to a general view of the factors affecting production.

[264] The experience of AFI, in its Winnipeg facilities, during the period between August 1996 and August 1997, was that 76 batches of AFI-4 were run with an average fermentation duration of 11 days. In other words, the optimization spoken of by Dr. Sailer for AFI-4 was reached by an 11-day fermentation.

[265] As we know, Blue Treasure began its runs of AFI-4 in June 1997. About 70 runs were made at Blue Treasure between June 1997 and October 1997. If the Batch Records are to be believed, although there is significant fluctuation, the average fermentation duration during that period was about 11 days. This was an expected result, given the experience of AFI with the AFI-4 process in Winnipeg.

[266] Blue Treasure shut down its production of lovastatin from October 1997 to March 1998. Other than 17 runs that took place between December 1997 and January 1998, there was no production of lovastatin in this period. Upon resumption of production in March 1998, the fermentation duration was immediately lower and eventually stabilized at nine days.

[267] These data were depicted by a graph, in Exhibit 83, prepared by Merck and presented to, and discussed by, a number of witnesses. What could account for the change in the fermentation duration?

[268] Merck’s explanation for the reduction in the fermentation duration after the plant shutdown is that Blue Treasure began to use the infringing AFI-1 process, instead of the AFI-4 process, to produce lovastatin.

[269] The graph was first presented to Dr. Cox during cross-examination. Dr. Cox, whose testimony was very credible and trustworthy, agreed with counsel for Merck that Exhibit 83 showed that the AFI's 11-day fermentation duration for AFI-4 was roughly consistent with the fermentation duration experienced by Blue Treasure up until the plant shutdown. He also agreed that the graph in Exhibit 83 depicted an average nine-day fermentation duration after the resumption of production at Blue Treasure in March 1998. Finally, and most importantly, Dr. Cox confirmed that the AFI-1 process transferred to Blue Treasure could be run in nine days.

[270] In my view, the decrease in fermentation duration after the Blue Treasure plant shutdown is more likely to have occurred with the production of AFI-1 lovastatin than with the production of AFI-4 lovastatin. Thus, even if the Batch Records are accepted as reliable evidence of the production runs, the data with respect to fermentation duration are consistent with the use of the AFI-1 process and not the non-infringing AFI-4 process.

(4) Increased Titres

[271] Fermentation duration is not the only variable to be considered in the economics of producing lovastatin. The amount of production or titres from each fermentation batch is of equal significance. Related to this issue is the role of Amicase in the fermentation medium. The AFI-4 process transferred to Blue Treasure required the use of a compound in the medium called Amicase**.** As I understand it, Amicase is an enzyme that is used as a catalyst in a chemical reaction. Dr. Connors testified that, "If you take out Amicase, then you get less lovastatin."

[272] Amicase was an expensive ingredient and the evidence suggests that Blue Treasure was taking steps to try to avoid its use. In a memorandum dated October 23, 1997 to Dr. Xinfa Xiao and Dr. David He, both employees of AFI, Mr. Huigen Xu, of Blue Treasure, explained that, when Blue Treasure tested fermentation without Amicase, they "did not find any effect on the product quality". However, the same memorandum reports a reduction in titres of 9.75% at the 12,800 L fermentation stage. Mr. Fowler confirmed that, although a loss of productivity of 9.75% was the result of removing Amicase from the medium, Blue Treasure could achieve a cost savings of about $224.00 US per kilogram by its elimination.

[273] From about January 1998, Blue Treasure produced lovastatin without using Amicase. One would logically expect that thereafter there would be a reduction in titres as reflected in the memorandum of October 23, 1997. That does not appear to have been the case.

[274] In Exhibit 103, Merck's counsel attempted to pull together all of the information on titres. This exhibit was prepared from Exhibit 149 (a complete set of the Blue Treasure Batch Records), and presented in graphical format in Exhibit 83. During three periods, the average titres recorded by Blue Treasure showed the following:

Period	Average titres (g/ml)
June 7, 1997 to October 27, 1997	2.3 (n = 53 runs)
December 8, 1997 to January 11, 1998	2.0 (n = 17 runs)
March 7, 1998 to October 7, 1999	2.2 (n = 292 runs)

[275] The chart demonstrates that there was a drop in titres of about 13% for the period December 8, 1997 to January 11, 1998. However, the titres increased, after the Blue Treasure plant shutdown, to a level approximately equal to the runs made with Amicase. The obvious

question is this: in the post-March 1998 period, how could Blue Treasure have obtained production levels without Amicase consistent with those with Amicase?

[276] Merck submits that the only reasonable explanation is that after March 7, 1998, Blue Treasure was using the AFI-1 process and not the AFI-4 process.

[277] In final oral argument, Apotex refers to a sub-set of the Batch Records to argue that there is no evidence that the omission of Amicase resulted in a reduction in titres. For support of this statement, they refer to Table A of Exhibit 156, listing "All L4-39-581 Fermentations Pre-March 1998." Apotex points out that the average titres of the three runs with Amicase are actually lower than in the 12 runs listed in Table A that were run without Amicase:

> The point is, using the same time point from the data, when you remove Amicase at nine days, you have a significantly better titre performance. So the argument, the argument that you would expect titres to go down, because they did remove Amicase in the later runs in March and following, is not borne out by this document which my friend put forward as Exhibit 156. It shows exactly the opposite.

[278] The problem with Apotex's submissions on this point is that the average of titres with Amicase highlighted by Apotex was based on an average of only three runs (September 24, 1997, September 26, 1997 and October 17, 1997). Apotex then compares this extremely small sample size against another small sample of 12 runs. In my view, the averages used by Apotex are based on a sub-set of the Batch Records from which relative conclusions as to titres for the entire Batch Records cannot be made.

[279] I prefer the information set out in Exhibit 103, which demonstrates an increase in titres of 13%. I accept that this is inconsistent with the omission of Amicase.

[280] Even discounting the effect of the omission of Amicase, there are inexplicable changes in production levels after the plant shutdown. This change in titres can be viewed in the context of L4-39-581, one particular strain of *Coniothyrium fuckelii* allegedly used both before and after the plant shutdown. From the Blue Treasure Batch Records, we can track the runs that Blue Treasure claims it used for this particular strain. Merck counsel prepared Exhibit 156 from the Batch Records. Table A of Exhibit 156 is a summary of the Batch Records for all runs using the L4-39-581 strain prior to the plant shutdown. Between September 24, 1997 and January 11, 1998, 15 fermentations were carried out. Although these batches ran for a duration of 11 days, we can calculate the hypothetical titres at nine days from the records. If these batches had been run for nine days, the average (arithmetic mean) titre would have been 1719 mg/L. Table B of Exhibit 156 consists of information from the Blue Treasure Batch Records for the alleged runs using the L4-39-581 strain after the plant shutdown. From March 7, 1998 to April 23, 1998, 19 runs were performed with an average fermentation duration of 8.3 days and an average titre of 2109 mg/L. This shows an increase of over 20% in titres.

[281] This increase is dramatic. Allegedly using the same strain of *Coniothyrium fuckelii*, L4-39-581, Blue Treasure managed to increase the productivity of the fermentation by over 20%. What explanation is there for the increase? Merck submits that the only reasonable explanation is that, for the runs after the plant shut down, Blue Treasure was not using a strain of *Coniothyrium fuckelii*, but was using a strain of *Aspergillus terreus*.

[282] In support of its belief, Merck referred to the testimony of Dr. Connors who was presented with scatter graphs representing the variations in titres among the Blue Treasure runs. Dr. Connors agreed that “one possible explanation” for a variation in titres before and after the plan shut down, could be the micro-organism or fungus used, when the medium and the process are kept constant. Dr. Connors did not specify what other explanations there could have been other than to say that something had to be different:

> What did you do in the middle that you didn’t do on either side? I wouldn’t necessarily say the culture has to be different, but something is different, obviously.

Dr. Connors provided no further assistance to the Court on what could explain the differences.

[283] The data replicated in some of the exhibits produced by Merck’s counsel from the Batch Records show that the variability in titres between runs diminished over time. I can accept, as a matter of common sense, the comments of Dr. Cox who explained that, “with the passage of time and the practice and the reproducibility and the adherence to the [Standard Operating Practices] and the ironing out of the problems”, there would be more consistency in titres. However, this does not account for the dramatic and immediate change in titres in evidence before me.

[284] The only witness presented by the Defendants who could speak to the dramatic change in titres was Mr. Luo. He was on the plant floor during the relevant times. According to the Defendants, Mr. Luo indicated that other changes to the fermentation conditions could result in a change of titres. Mr. Luo spoke about possible changes to aeration, pressure, the media and agitation, and about increased familiarity with the process. However, when Mr. Luo’s testimony is examined, only one explanation – increased agitation – is really offered. And, I have difficulty with that explanation.

[285] Exhibit 156 was presented to Mr. Luo during cross-examination. He was asked what could have explained the increased titres after the plant shutdown. Mr. Luo testified that a 23% jump could be justified as follows:

> A 23 percent jump, it's not necessarily like by changing the [strains]. It can also be changed by optimizing the fermentation conditions of the medium.
>
> . . . There is lots of factors. It is not only the strain.
>
> As the staff, the production staff, get more familiarized with the production procedure and techniques, and then they get improvement on that, it will also change.
>
> So even for the same strain and the different batches, even for the same strain, the different batches may also have a different – like, a different result in titre.

[286] When questioned, Mr. Luo suggested that a change in aeration could improve production. However, he was unable to point to any change in aeration from the pre-shutdown runs to the post-shutdown runs.

[287] Mr. Luo explicitly agreed that there was no change in pressure.

[288] With respect to a change in medium, Mr. Luo was questioned about the removal of Amicase. His explanation was bewildering. While he acknowledged that removing Amicase would probably reduce the titres, he stated that the removal of Amicase would not necessarily reduce titres. This runs counter to other testimony on the issue and to common sense.

[289] At the end of the line of cross-examination on the issue of increased titres, the only possibly concrete suggestion from Mr. Luo was that increased agitation during the fermentation could account for the 23% rise in titres.

[290] Apotex argues that a change in agitation could indeed explain the change in titres. Apotex first refers to production parameters set out in Exhibit 49 where a cultivation condition of "agitation between 100 and 130 (depending on DO)" is set out for AFI-1. In contrast, Apotex notes that the agitation described in the Batch Records for AFI-4 is closer to 170. Moreover, Apotex points to Exhibit 94, an AFI comparative report where it is reported in section 5.5 that, "for most of fermentation time, less vigorous agitation is needed for AFI-1 compared to AFI-4."

[291] I give no weight to the information contained in Exhibit 49 referred to by Apotex. First, the document appears to have been produced no later than spring of 1995 as part of the transfer of technology related to AFI-1 lovastatin from AFI to Blue Treasure. I have no idea of what the ultimate instructions followed were and no explanation of why an agitation of 100 to 130 should be used. I also observe that the document is made subject to the note that:

> This is a preliminary document and <u>many process parameters including agitation</u>, aeration, media volumes, cultivation durations, feeding amounts and frequencies etc. <u>are subject to additional adjustments during the validation runs.</u>
>
> [Emphasis added.]

Beyond the Batch Records, I have no information on what the actual agitation levels for AFI-1 in production were or should have been. This document does not assist me.

[292] I also give no weight to the statement contained in section 5.5 of Exhibit 94. Exhibit 94 is an untitled document that was produced by AFI during the pre-trial litigation. The document appears to relate to differences between the AFI-1 and AFI-4 processes. It was referred to by counsel for Merck during cross-examination of Dr. Sailer. Dr. Sailer described the document as "some kind of R & D report possibly" and admitted that he had never seen the document. Although Dr. Sailer was questioned on some of the contents of this document, I have no idea who is the author of this document or whether section 5.5 is accurate.

[293] That leaves Apotex's analysis of the Batch Records as the only support for the increased agitation argument. I acknowledge that there appears, in general, to be an increase in agitation after the plant shutdown. However, I have no reliable evidence that would support Mr. Luo's statement that an increase in agitation explains the dramatic increase in titres.

[294] This leaves me with no credible explanation for the post-shutdown increase in titres other than a change in organism. Thus, even if the Batch Records are accepted as reliable evidence of the production runs, the data with respect to titres are consistent with the use of the AFI-1 process and not the non-infringing AFI-4 process. In spite of the removal of Amicase and a decrease in fermentation duration, Blue Treasure managed to obtain increased titres. The only explanation consistent with the evidence before me is that Blue Treasure was using a different micro-organism – *Aspergillus terreus*.

(5) Motivation, Means and Opportunity

[295] Supporting the arguments above, Merck also submits that Blue Treasure had the motive, means and opportunity to make and ship infringing lovastatin to AFI.

(a) *Motivation*

[296] First, Merck asserts that Blue Treasure had a significant financial motivation to make infringing lovastatin that it would then sell to AFI. A number of facts certainly appear to support this argument:

- the financial difficulties prior to the introduction of AFI-4;
- the problems with the production of lovastatin using AFI-4; and
- the inability of Blue Treasure to make a profit at the Blue Treasure Joint Venture contract price.

[297] Financial problems at Blue Treasure appear to have existed even before the production of AFI-4 lovastatin. As we know, Blue Treasure was expected to sell AFI-1 lovastatin in China or other foreign markets. The Minutes of the 6th Meeting of the Board of Blue Treasure held August 26-27, 1996 described the difficult market conditions in China and indicated serious financial problems at Blue Treasure. At that time, unpaid loans and utilities bills would leave

Blue Treasure with no funds to produce the planned lovastatin. Dr. Cox, during cross-examination, acknowledged that, at that time, the outlook was not "very promising".

[298] A concern for Blue Treasure from early 1997 was the challenge of selling into the Chinese market. In a memorandum, dated March 7, 1997, Mr. Zhou referred to the "less than satisfactory" sales of lovastatin in China and commented as follows:

> In domestic market, there is a fierce rivalry market of Bulk Lovastatin course price to decline. As far as we know, ZeJing province Hai Mei Pharm. Offered the price of Bulk Lovastatin is RMB thirty-two thousand [approximately $3,900 US as confirmed by Mr. Fowler (T4565)] for one kg. If we do that, we will difficult to subsist. [Emphasis added.]

[299] Mr. Fowler, who was responsible for financial matters at AFI during the relevant times, confirmed that RMB 32,000 would convert to approximately US $3900. In the absence of any other evidence on the pricing economics, I accept that Blue Treasure's "break even" price for the sale of lovastatin was about US $3900.

[300] The financial difficulties of Blue Treasure apparently were worsened by the refusal of AFI to provide higher-yielding strains of *Aspergillus terreus*. In the same memorandum referred to above, Mr. Zhou "urgently" requested that AFI provide it with an improved strain or "super fungus". Since Mr. Zhou did not testify at the trial, I can only assume that he believed that a better strain of *Aspergillus terreus* would have helped Blue Treasure's dire financial situation. AFI did not respond to this request from Blue Treasure. Dr. Cox acknowledged the refusal:

> Q. You had a contract, after having given them that strain, which obliged you to give them all of the improvements, correct?
>
> A. Correct.

> Q. You were withholding that, despite your certain knowledge of their financial situation?
>
> A. Yes
>
> Q. And despite the contractual obligations?
>
> A. If they were able to sell material with the old strain we might have considered doing that. There's no point in transferring a high performing strain when they can't sell the bulk material.

[301] The decision to send the AFI-4 micro-organism to Blue Treasure was made, at least in part, to allow Blue Treasure to make non-infringing lovastatin that it could sell on the Canadian market. In spite of this, the evidence before me shows that Blue Treasure had some difficulties with producing lovastatin with the strain of AFI-4 sent by AFI. The result was that the financial picture for Blue Treasure did not improve.

[302] Blue Treasure's experience with AFI-4 was troubled. Wide fluctuations in batch-to-batch titres were observed at Blue Treasure prior to March 1998. As acknowledged by Dr. Cox, running a plant economically and efficiently requires a range of variability within acceptable limits; variability outside the acceptable range would make it harder to earn a profit. A memorandum, dated August-13, 1997, from Mr. Zhou to Dr. Cox highlighted the difficulty:

> Because the fermentation viscosity of new AFI process have a great fluctuation, some equipment in downstream didn't suit for the new technology and brought many difficult for downstream.
>
> [Emphasis added.]

[303] Blue Treasure also experienced difficulties with some of the AFI-4 strains provided by AFI. In a memorandum dated October 20, 1997, Mr. Zhou noted that a replacement strain for L4-42-581 showed only 50% of the productivity and:

> Therefore, it can't be used for production. Also the strain L4-39-581 was not satisfactory for production: titers of shake flask test and fermentation showed more than 20% productivity reduction will occur if Strain L4-39-581 is used compared to that of Strain L4-42-581. This will certainly affect margin of cost and price.

[304] Mr. Zhou requested that AFI send "100 frozen vials of L4-42-581 or vials with similar productivity or higher". The request for more vials of L4-42-581 was repeated by Dr. Su in an e-mail dated October 19, 1997. As confirmed by Mr. Primrose, a shipment of seed vials that included 10 vials of L4-42-581 was sent by AFI to Blue Treasure on August 4, 1998. I have no other evidence of any response to the request of Blue Treasure for a better AFI-4 strain.

[305] Apotex asserts that the fact that Blue Treasure was requesting additional information and a better AFI-4 strain is inconsistent with Merck's hypothesis that Blue Treasure was, in fact, using the infringing process after March 1998. Given that Mr. Zhou, the author of most of the memoranda relied on by Apotex, did not testify in this trial, I have no way of determining whether Apotex's theory is believable.

[306] As noted above, Blue Treasure was concerned about being able to subsist with pricing of about US $3900 per kg for *Aspergillus terreus* lovastatin. Considerable evidence was produced at trial to demonstrate that the costs of producing AFI-4 would be higher and that the profit margins even smaller.

[307] As stated in a lengthy AFI Monthly Scientific Report, dated July 3, 1997, in which the AFI-1 and AFI-4 processes were compared, “The calculated cost of production of AFI-1 was significantly less than the production costs for AFI-4.” The same document stated that the media ingredients were the single most significant cost factor.

[308] The offer to transfer the AFI-4 process to Blue Treasure and to purchase AFI-4 lovastatin was outlined in a letter dated April 10, 1997 from Dr. Cox to Mr. Zhou. As confirmed by Dr. Cox, Blue Treasure initially asked for US $6000 per kg. AFI agreed to pay only US $4500 to US $5000, depending on the average titres. A price of US $4500 would be about $600 to $700 over Blue Treasure’s “break even” price of US $3900 per kg. However, the margin would have been significantly eroded by the added costs of the AFI-4 media ingredients and by having to meet AFI’s 0.2% RC-14 specification. Moreover, over the course of the batches sold to AFI, the purchase price dropped to US $3300 per kg.

[309] The result is that, if Blue Treasure had been using the AFI-4 process, it would have been losing significant amounts of money for each kilogram of product shipped to AFI. Blue Treasure could not have made a profit by selling AFI-4 lovastatin to AFI at the price AFI paid. However, the evidence of Mr. Fowler was that, once Blue Treasure began to use the AFI-4 process, they “worked their way out of the financial difficulties and became profitable”. Quite simply, there is no evidence on the record that explains how Blue Treasure could have turned a profit using the AFI-4 process.

[310] I conclude that Blue Treasure had financial motivation to use the AFI-1 process instead of the non-infringing – but more costly – AFI-4 process.

(b) *Means*

[311] The ability or means of Blue Treasure to produce the quantities of AFI-1 lovastatin depends, at least to some extent, on the availability of the appropriate strains of AFI-1.

[312] Apotex argues that it was not shown that Blue Treasure had such a strain. Apotex refers to the production master batch records provided to Blue Treasure as part of the *Aspergillus terreus* technology transfer. In production, the strain showed titres generally below the 1.5 g/L level. Not only was the titre level well below 2.0 g/L reflected in the Batch Records, but the stated fermentation time was 12 to 15 days – a longer period than reported in any of the post-March 1998 runs. Merck does not agree.

[313] Merck submits that Blue Treasure was in possession of a high-producing strain of AFI-1 giving it the means to make additional AFI-1 lovastatin with the very titres reflected in the Batch Records after March 1998 when the average titres were about 2.2 g/L. The reference to this strain is contained in the Management Report for the 6th Meeting of the Board of Directors of the Blue Treasure Joint Venture held on August 26-28, 1996. In that document, at paragraph 1.3, the titres are stated to be 2300 to 2500 mg/L. Moreover, a document entitled “Historical review of Lovastatin production improvement *Aspergillus* sp. and *Conioth[y]rium fuckelii* strains in R&D Biology” states that AFI achieved up to 5100 mg/L. When Mrs. Hu was asked whether Blue

Treasure had an AFI-1 strain that produced titres in the range of 2300 to 2500 mg/L, she claimed to be unable to know what the question was about. This response is surprising given Mrs. Hu's responsibilities for the security of various strains of both AFI-1 and AFI-4 and for inoculating the initial fermentations for each batch.

[314] With respect to fermentation duration, the evidence of Dr. Cox was that the AFI-1 strain transferred could be run in nine days.

[315] Although there appears to be some contradictory evidence, I conclude that it is more likely than not that Blue Treasure had a strain of AFI-1 that could have met the titres and fermentation durations reflected in the Batch Records after March 1998.

[316] I am persuaded that Blue Treasure had the means to produce lovastatin with the infringing AFI-1 process.

(c) *Opportunity*

[317] The final element examined by Merck is opportunity.

[318] As described earlier in these reasons, Dr. Jerry Su was sent to Blue Treasure to investigate certain problems with the initial AFI-4 runs. Dr. Su arrived in China on August 25, 1997 and returned to Winnipeg on October 31, 1997. Dr. Su expressed his opinion that the runs he observed were carried out in accordance with the Standard Operating Procedure for AFI-4.

However, as confirmed by Mr. Fowler, after Dr. Su's departure in October 1997, no one was ever sent from AFI to assess the production. AFI apparently assumed that Blue Treasure would follow the instructions that had been provided in spite of earlier problems.

[319] AFI also missed another chance to identify the micro-organism used by Blue Treasure. As confirmed by Ms. Christofalos, with each shipment of product to AFI, Blue Treasure sent a sample consisting of a mycelial or fungal cake. Dr. Connors opined that such product could have been subjected to DNA testing for the presence of the non-infringing *Coniothyrium fuckelii*. However, the fungal cake was never tested and was, unfortunately, destroyed during the course of this litigation.

[320] Blue Treasure had the opportunity to revert to manufacturing AFI-1 as soon as Dr. Su left at the end of October 1997.

(6) Blue Treasure Conduct

[321] Merck submits that the behaviour of Blue Treasure raises serious doubts about the Defendants' allegations that there has been no infringement. One of the most serious and disturbing stories involves two articles published in the Chinese Journal of Antibiotics. Merck argues that these two articles are direct evidence that Blue Treasure used *Aspergillus terreus* to manufacture lovastatin, most likely in late 1997. Furthermore, the behaviour of Blue Treasure's employee, Mr. Luo, in association with the articles, provides evidence that Blue Treasure is prepared to go to great lengths to cover up its infringing activities.

[322] In early 1999, an article entitled “Optimization of Formula for Lovastatin Fermentation Medium through Uniform Design” was published in the Chinese Journal of Antibiotics, February 1999, Vol. 24, No. 1 (referred to as Article #1). One of the authors of this article was listed as “LUO Dingjun”. Mr. Luo who appeared as a witness in this trial is the same Mr. Luo who wrote this article. As set out in the abstract of Article #1, the authors were presenting a method of optimizing a fermentation medium for producing lovastatin. In summary terms, the authors conducted experiments to ascertain the effectiveness of replacing two “extremely expensive” raw materials – Peptone and Amicase – in the fermentation medium with domestically produced raw materials. One of the replacement products was a fish powder, giving rise to a reference, during this trial, to the experiments as the “fish powder experiments”.

[323] Article #1, in its abstract, contains the following sentence:

> The company [Blue Treasure] has imported patented lovastatin production technology from Canada, with the fermentation medium formula being a United States patented (patent number 5409820) formula.

[324] The reference to “patent number 5409820” is most likely a reference to United States Patent No. 5, 409, 820 issued to Apotex Inc. on April 25, 1995. This patent claims a process for making lovastatin using *Coniothyrium fuckelii*. In spite of this reference at the beginning of Article #1, there is no further reference to *Coniothyrium fuckelii*. Indeed, the article explicitly states that the fish powder experiments were conducted on the “Lovastatin-producing strain *Aspergillus terreus* BN 270-001.” There is no reference in Article #1 to the use of a *Coniothyrium fuckelii* strain of lovastatin. The article also describes Guangdong Blue Treasure Pharmaceutical Co. Ltd. as the company who was producing lovastatin in China and the

company that was interested in the lowering of the costs of the fermentation medium for lovastatin.

[325] A second article, entitled “A Study Regarding Lovastatin-Producing Strain Protoplast Mutation and Fermentation Formula Optimization,” was published in the Chinese Journal of Antibiotics, October 2000, Vol. 25, No. 5 (referred to as Article #2). Mr. Luo was also one of the authors of this article. The purpose of Article #2, as reflected in the abstract, was to produce a high-yield strain of lovastatin “by mutating lovastatin-producing strain protoplasts” and optimizing the fermentation culture medium formula. Once again, the authors listed, as the strain used for their experiments, “lovastatin-producing strain *Aspergillus terreus* (BN 270-053)”. In Article #2, there is no mention of the US Patent.

[326] Dr. Luo testified that the shake flask experiments (referred to in Article #1 and #2) were performed at Blue Treasure’s microbiology lab.

[327] These articles raise a strong inference that, at the time of the experiments, Blue Treasure was producing lovastatin from *Aspergillus terreus* at its facility.

[328] Mr. Luo was asked about the two journal articles during his examination-in-chief. In response to a question on the purpose of publication, Mr. Luo responded that:

> Getting this paper published is mainly for the technicians being able to get certified. Basically it's a kind of when you come to a profession new to get certified, certification.

[329] Mr. Luo was unable to remember clearly when the experiments were run, but he thought that they were carried out in 1997 “between summer and fall of that year”. Mr Luo further testified as follows:

> Q. Where was these experiments conducted?
>
> A. These experiments are done at Blue Treasure's micro-biology laboratory.
>
> A. Specifically what strain was used I can't remember so clearly, but looking through this article probably I used number 4 strain.
>
> Q. Why does it say Aspergillus terreus was used?
>
> A. Because at that time due to the confidentiality reasons I don't want to leak the secrets about AFI-4 strain.

[330] I find Mr. Luo’s testimony related to these two articles to be astounding. First, it is simply incomprehensible that a group of scientists would fabricate a journal article to hide the identity of the *Coniothyrium fuckelii* fungus. Beyond a bald assertion, Mr. Luo presented no cogent reasons as to why the use of *Coniothyrium fuckelii* would have been confidential.

[331] I also question Mr. Luo’s testimony with respect to when the experiments were conducted. His lack of memory is surprising. Mr. Luo has known about the significance of these articles for some time and yet was unable to recall the dates of the experiments. He could have refreshed his memory in a number of ways before testifying. Instead, he expressed the view that the experiments were done in the period of time before the use of the AFI-4 process. His faulty memory, in my view, is consistent with fabrication, by Mr. Luo, of what organism was being used at Blue Treasure in the time leading up to the publication of the articles.

[332] The two articles contain other references that discredit Mr. Luo's claims. First, the strain used for the articles was described as BN 270-053. In the opinion of Dr. Lasure, this was a reference to the 53rd isolate of *Aspergillus terreus* BN-2-70. This is the same strain obtained from AFI as AFI-1 (Lasure Expert Report, Exhibit 48, para. 242).

[333] The second area of disconnection relates to the ability of the strains of *Coniothyrium fuckelii* used in AFI-4 to sporulate. The evidence of Dr. Cox was to the effect that, in his experience working at AFI, the strain of *Coniothyrium fuckelii* transferred to Blue Treasure had lost the ability to produce spores during fermentation:

> Q. All right. You know that at some point Coniothyrium fuckelii ceased sporulating at AFI?
>
> A. Yes, I believe so.
>
> Q. That makes it harder to prepare and maintain consistent seed banks from generation to generation?
>
> A. A little bit, yeah.
>
> Q. That cessation of sporulation is a property of the organism?
>
> A. Not of the organism, no, it was an effect of the mutagenic strain improvement program that AFI performed.
>
> Q. The non sporulating character became intrinsic to Coniothyrium fuckelii as a result of that program, is that fair?
>
> A. That strain of Coniothyrium fuckelii, yes.
>
> Q. Right.
>
> A. It's not an inherent characteristic of the species.

> Q. Got it. Never a problem that was encountered with Aspergillus terreus?
>
> A. No.
>
> [Emphasis added.]

[334] In spite of the information that the AFI-4 strain sent to Blue Treasure could not sporulate, in Article #2, at section 1.2.3, the authors explicitly report as follows:

> Investigation of strain-producing capacity: The spores on the mature PDA slants are washed, inoculated onto a rice culture medium, and cultured for 7 days, yielding mature rice spores.

[335] In sum, Mr. Luo's explanation about why he lied in the two articles is not believable. Mr. Luo fabricated his testimony before this Court to cover up the use of *Aspergillus terreus* at a time when Blue Treasure was supposed to have been exclusively using the AFI-4 process. The better explanation for these two articles and Mr. Luo's testimony is that the fish powder experiments were carried out on lovastatin using AFI-1. I find that, on a balance of probabilities, the experiments were carried out with the AFI-1 process (that is, with *Aspergillus terreus*). It follows that the two articles support Merck's claims that Blue Treasure was using *Aspergillus terreus* to make lovastatin and thus infringing the '380 Patent.

C. *Conclusion on Blue Treasure Circumstantial Evidence*

[336] Most of the foregoing evidence could be characterized as circumstantial evidence and requires that I draw inferences to reach the conclusion that, on a balance of probabilities, there was infringement.

[337] With respect to the drawing of inferences, Apotex argues that I must avoid relying on alleged inferences that are no more than speculation. I agree.

[338] Obviously, there is a difference between reasonable inference and pure conjecture. The Federal Court of Appeal provided the following comments in an appeal of an immigration judicial review, in *Minister of Employment and Immigration v. Satiacum* (1989), 99 N.R. 171 at p. 179, [1989] F.C.J. No. 505 (QL)(F.C.A.):

> The common law has long recognized the difference between reasonable inference and pure conjecture. Lord Macmillan put the distinction this way in **Jones v. Great Western Railway Co.** (1930), 47 T.L.R. 39 at 45, 144 L.T. 194 at 202 (H.L.):
>
> > The dividing line between conjecture and inference is often a very difficult one to draw. A conjecture may be plausible but it is of no legal value, for its essence is that it is a mere guess. An inference in the legal sense, on the other hand, is a deduction from the evidence, and if it is a reasonable deduction it may have the validity of legal proof. The attribution of an occurrence to a cause is, I take it, always a matter of inference.
>
> In **R. v. Fuller** (1971), 1 N.R. 112 at 114, Hall J.A. held for the Manitoba Court of Appeal that "[t]he tribunal of fact cannot resort to speculative and conjectural conclusions." Subsequently a unanimous Supreme Court of Canada expressed itself as in complete agreement with his reasons: [1975] 2 S.C.R. 121 at 123, 1 N.R. 110 at 112.

[339] In the case before me, I am satisfied that I am not relying on conjecture or mere guess; rather, the deduction from the totality of the evidence that Blue Treasure was manufacturing lovastatin using the infringing AFI-1 process is reasonable and logical.

[340] Given the extent of the evidence before me and the lack of alternative, reasonable explanations for much of that evidence, I find that Merck has satisfied its burden to show that it is more likely than not that, from March 1998, Blue Treasure was manufacturing lovastatin using the infringing AFI-1 process. The lovastatin was then delivered to AFI for ultimate sale into the Canadian market. This constituted infringement of the '380 Patent.

[341] This conclusion stands without any reference to the DNA evidence. That is, regardless of whether the DNA evidence presented by Merck constitutes reliable evidence of direct infringement, I find that any amount of lovastatin manufactured and sold in Canada that used lovastatin produced by Blue Treasure after March 1998 infringed the '380 Patent.

[342] The DNA evidence is dealt with in section VIII of the Reasons.

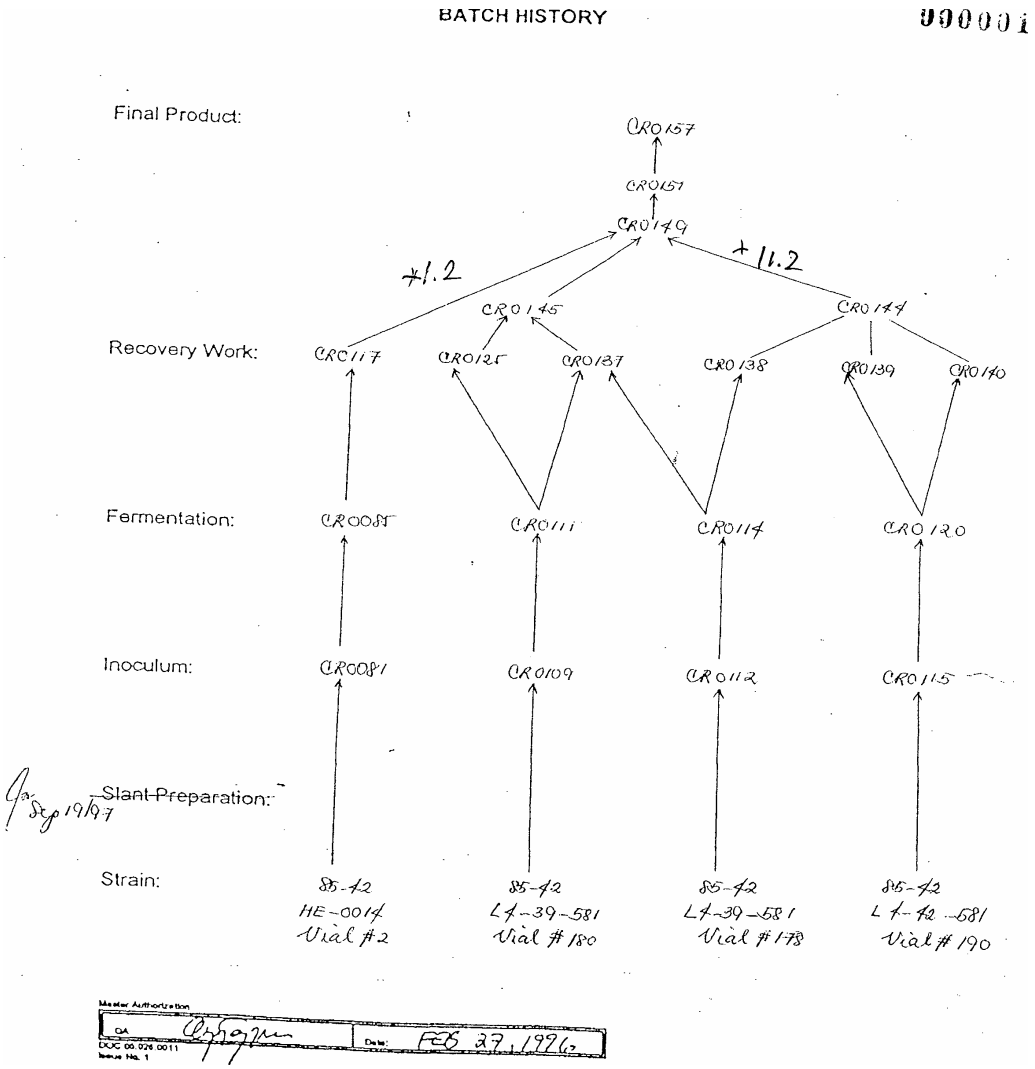
D. *AFI Batch CR0157*

[343] Merck no longer claims that all of the lovastatin produced in Winnipeg by AFI infringed the '380 Patent. However, Merck continues to assert that one batch of lovastatin – referred to as CR0157 – contained lovastatin that was made using the process protected by the '380 Patent.

[344] Batch CR0157 consisted of 12.57 kg of USP-grade lovastatin. It was manufactured at AFI in Winnipeg and sent directly to the attention of Dr. Barry Sherman at Apotex Inc. on December 2, 1996. It was the first batch of AFI-4 lovastatin shipped to Apotex Inc.

[345] The batch history reflects that CR0157 was the final crystallization of CR0151 which, in turn, was a recrystallization of CR0149. CR0149 was the crystallization of three extraction batches: CR0117, CR0145 and CR0144. The "genealogy" of batch CR0157 was confirmed by Dr. Sailer, during his examination-in-chief, and is depicted in Figure 1 below.

Figure 1



[346] The essence of Merck's argument is that CR0157 was a combined batch of non-infringing and infringing lovastatin. The key evidence relied on by Merck is:

(1) AQA 94 Batch Records (referred to as AQA 94) show that CR0157 was "AFI#1,4 FLAGGED contains top secret material" which would indicate it was a mixture of *Aspergillus terreus* and *Coniothyrium fuckelii* lovastatin;

(2) Some of the batches that ultimately resulted in batch CR0157 (specifically CR0151, CR0117, CR0144 and CR0149) show significant alterations that increased the weights of lovastatin from those initially recorded.

(3) The DNA testing carried out by Dr. Davies demonstrated that tablets of Apo-lovastatin tested positive for *Aspergillus terreus* and negative for *Coniothyrium fuckelii*.

[347] In my view, for the reasons that follow, neither of the first two arguments is persuasive on its own. However, the direct evidence of *Aspergillus terreus* in tablets made from the CR0157 batch was uncontradicted and provides direct evidence of infringement.

[348] As part of the trial record, the Defendants produced AFI's batch records. These records were obviously produced contemporaneously with the fermentations to which they refer and were kept in AFI's normal course of business. In contrast to the Batch Records for Blue

Treasure, the AFI batch records are acceptable as business records. In other words, the AFI batch records are *prima facie* proof of the facts stated therein.

[349] However, it does not follow that every document, produced by AFI, that looks like a business record meets the strict criteria to be admitted into evidence as a business records. This is particularly true with the document referred to as AQA 94 and relied on by Merck.

[350] AQA 94 is a one-page document consisting of a list of 56 batch numbers with brief notations. The entry of interest is at line 11:

> CR0157 AFI#1,4 FLAGGED contains top secret material.

[351] The document was introduced to Dr. Cox who was unable to identify it or to provide any testimony that could have assisted the Court. Ms. Christofalos was asked about the document during her examination-in-chief.

> Q. Are you able to identify this document?
>
> A. This looks like one of our internal, well, it is one of our internal record-keeping documents where we just have made an index of a bunch of documents that is going into a box.
>
> Q. Do you know what purpose was made for it?
>
> A. Just for filing purposes.
>
> Q. Do you know when it was made?
>
> A. We started this exercise late 99. I would, that's my recollection, late 99.
>
> Q. Can you tell the Court who made it?
>
> A. Could have been any number of people, most likely our records clerks.

[352] Although Ms. Christofalos admitted that she did not prepare the document, she expressed her view that the list was merely an identification of boxes of documents. Further, Ms Christofalos provided what, in my view, was a reasonable explanation of why there was the reference to "AFI#1,4" in the document:

- The person making this list would have looked at the first page of the actual Interim Production Batch Record and would only have seen "Product Name: lovastatin USP" and "Product Part Number: 6000".

- Part number 6000 applied to lovastatin made with either AFI-1 (*At*) or AFI-4 (*Cf*), thus leading to the entry listing both.

- The reason why the error was never corrected was because these lists were not control documents.

[353] With all respect to Merck, I fail to see how this document of dubious origin can be strong circumstantial evidence of an infringing product in a batch of lovastatin. Dr. Cox was clearly unaware of AQA 94. Ms. Christofalos's explanation was simply that this was an index of documents. She did not prepare the list and was unsure of who could have prepared it. The list of documents was only made in 1999 – more than two years after batch CR0157 was manufactured. Unlike the AFI batch records, AQA 94 does not qualify as a business record. I do not accept it for the truth of its contents – in particular, that CR0157 was a mixture of infringing and non-

infringing lovastatin. In light of the lack of connection between AQA 94 and the “genealogy” of CR0157, I give no weight to this document.

[354] The only remaining argument of Merck (other than the DNA evidence) relates to some apparent anomalies surrounding the weight of the three preliminary batches that ultimately became part of CR0157. In making this argument, Merck refers to the batch records for three antecedent downstream batches: CR0151, CR0117 and CR0144. In each case, a document that forms part of the batch records shows a manual change to the originally-recorded weight of the material obtained. In each case the weight was increased. In Merck’s submission, the augmentation is consistent with the addition of infringing lovastatin to the batch.

[355] In response, the Defendants attempted to provide an explanation for these discrepancies through the evidence of Dr. Sailer and Ms. Christofalos.

[356] Dr. Sailer clarified that the antecedent weights going into CR0157 cannot simply be added up, as it is a weight loss process.

> Q. Right. Well again, I don't have any errors to complain about there either. The only point I guess I'm conceding, and I want to make sure I understand that I have it right, is that we can't simply add together these three numbers?
>
> A. We can because the batch 151 was generated from batch CR0149 and those two errors which we see in the material coming to batch CR0149, which you said it's plus 11.2 plus 1.2 kilograms, generated certain quantity.
>
> Q. Right.
>
> A. As a starting material for the next batch 151. During the next batch when they tried to discharge it they have to correct it

> because they discharge extra 3.8 kilograms, which actually doesn't matter at all because if they didn't discharge it, we will dissolve it anyway and mix it with the 11.11 kilograms to generate 14.8 kilograms of product, which was starting material for the batch 157 of the final product.
>
> Q. All right.

[357] Further, at a later date, extra lovastatin was found that had been captured in the filter, which was not initially observed by the operators. It was subsequently recorded. Dr. Sailer points out that the crossed out weights were the result of mistakes by inexperienced technicians.

> Q. All right. So let's go to tab three, page 82. Have you got that page?
>
> A. Yes.
>
> Q. And I'm seeing a table one crude Lovastatin obtained, do you see that?
>
> A. Yes, I do.
>
> Q. And I see the first listing is CR0117?
>
> A. I can see it.
>
> Q. But I see the net weight is 3.8 kilograms.
>
> A. Yes.
>
> Q. What explanation, if any, do you have for the Court for that?
>
> A. I have similar explanation. This is first batch which was filtered on this equipment, NF 1, and this is what they found when actually they dismantled the screen, they dropped the bottom and they found there was still product there. I know it should be recorded here but as I said it was first batch. And yeah, we didn't have really experience. We were quite new crew there, so yeah, it's missing, missing note that additional 1.2 kilogram was found on the screen.

[358] Finally, I observe that the corrections to the records were made some eight days after the original entry. When asked about the delay, Dr. Sailer was unable to provide a response.

[359] While the explanations given by Dr. Sailer and Ms. Christofalos could provide a sufficient answer for the discrepancy, they are only that - an explanation or hypothesis. Their answers do not explain why there was an eight-day delay in changing the document or provide a fulsome explanation of how the process of making lovastatin would “lose weight”.

[360] In sum, I am left with unanswered questions on the make-up of batch CR0157. Since the batch was never tested by Apotex, I have no direct evidence that the batch was not *Aspergillus terreus* lovastatin. However, in the submission of Merck, I do have direct evidence that tablets from the CR0157 batch were made from infringing lovastatin. Merck makes this argument based on the DNA testing results of Dr. Davies. That evidence is considered in section VIII of these Reasons.

VIII. Infringement – the DNA Evidence

A. *Introduction*

[361] Merck’s case on the direct evidence of infringement rests on the DNA testing carried out on behalf of Dr. Julian Davies in his laboratory at the University of British Columbia (referred to as the Davies Lab). Merck relies on the Expert Report and testimony of Dr. Davies to assert that

there is direct evidence that lovastatin manufactured by Blue Treasure and lovastatin contained in AFI batch CR0157 contained *Aspergillus terreus*, thereby infringing the '380 Patent.

[362] Dr. Davies received and tested three samples of lovastatin, consisting of: (a) three vials of white powder and one vial of brown powder, purporting to be samples from Blue Treasure provided through the services of Mr. Ted Kavowras; and (b) Apo-lovastatin tablets made from AFI batch CR0157.

[363] Two sets of experiments were carried out at the Davies Lab on the same samples – the first in 2003 and another in 2007. In 2003, the experiments were performed by Karen Lu, a senior technician for the Davies Lab. In 2007, Grace Yim, a Ph.D candidate in the Davies Lab, assisted Karen Lu in performing the experiments.

[364] In 2003, the experimental procedure involved a number of steps: DNA was extracted from the samples; specific primers diagnostic of the fungi region in DNA were chosen from the published literature; the primers were used to amplify the DNA in a nested polymerase chain reaction (nested PCR); the amplified DNA was subjected to gel electrophoresis; and then the gel was stained and analyzed under ultra-violet (UV) light for the presence of DNA. The UV light analysis highlighted the presence of bands which correlated to 130 base pairs (bp). These bands were determined to be a positive “hit” for *Aspergillus terreus* DNA. The bands were extracted from the gel and sent to a lab which specializes in DNA sequencing. The Davies Lab compared the results of the DNA sequencing to the sequence for *Aspergillus terreus* DNA that is located in

the database at the National Institute for Biotechnology Information. This comparison confirmed that the DNA "hit" in the lovastatin samples was, in fact, *Aspergillus terreus* DNA.

[365] In 2007, the Davies Lab repeated the experiments with a modified procedure and tested for the presence of both *Aspergillus terreus* and *Coniothyrium fuckelii* DNA. Again, a positive result was only found for *Aspergillus terreus*.

[366] The combination of the experiments performed in 2003 and 2007 resulted in 13 positive findings of *Aspergillus terreus* DNA, and no positive findings of *Coniothyrium fuckelii* DNA. Based on these results, Dr. Davies opined that the fungus responsible for producing the lovastatin in the samples tested by the Davies Lab was *Aspergillus terreus*.

[367] The first general and critical consideration is that the burden that falls on Merck is one of a balance of probabilities. That is, Merck succeeds if I am satisfied that it is more likely than not that the samples tested contained *Aspergillus terreus* DNA.

[368] A number of issues arise with respect to the DNA evidence presented through Dr. Davies:

1. Is there a nexus between the Blue Treasure samples tested and the Blue Treasure lovastatin that is alleged to infringe the '380 Patent?

2. Should the results of the testing in the Davies Lab be rejected because they were not reproducible by Dr. Poinar?

3. Does the failure of Dr. Davies to find *C. fuckelii* DNA in the tablets from batch CR0157 support Apotex's position that his DNA evidence is unreliable?

4. Is "ancient DNA" the same as, or analogous to, the DNA that would be found in the samples tested by Dr. Davies?

5. Should the results of the testing in the Davies Lab be rejected because the *Aspergillus terreus* DNA found in the Davies Lab was the result of contamination by exogenous DNA?

6. Should the weight to be given to Dr. Davies's Expert Report and his opinions be reduced due to:

    a) the inability to describe elements of the experiments reported in his Expert Report;

    b) the incomplete reporting of the experiments conducted in the Davies Lab;

    c) the failure to disclose the majority of tests relied on; or

d) the failure to use negative extraction controls?

[369] To this list, I would add the issue of the weight to be given to the opinions of the experts put forward by Apotex – Drs. Gilbert, Poinar and Taylor. Should the narrow expertise of these witnesses reflect on the weight to be given to, or the relevance of, their opinions?

B. *Nexus between the samples tested and the allegedly infringing lovastatin*

[370] An assessment of the DNA evidence in this case necessarily begins with the source of the samples that were tested in the Davies Lab. The presence of *Aspergillus terreus* in the samples only establishes infringement if the samples were obtained: (a) from lovastatin that was manufactured by Blue Treasure during the relevant time period; or, (b) from Apo-lovastatin tablets whose source was AFI batch CR0157.

[371] I begin with the three vials of white powder and one vial of brown powder allegedly obtained from Blue Treasure. In 2000, a law firm representing Merck hired Mr. Ted Kavowras to obtain samples of Blue Treasure lovastatin. Mr. Kavowras has an investigative consulting firm based in China called Panoramic Consulting. Most of his investigations are done undercover. Mr. Kavowras has considerable experience obtaining evidence used in civil litigation.

[372] Mr. Kavowras testified that, using the alias of “Mr. Garcia”, he approached Blue Treasure to obtain lovastatin samples. In October 2000 and January 2001, he obtained samples from an employee of Blue Treasure. Samples, from two batches, were delivered in a sealed

package with a corresponding certificate of analysis for each of the two samples - recorded as batch numbers 200012016 and 200012015. During his testimony at trial, Mr. Kavowras confidently identified the exhibits produced as the samples that he obtained from Blue Treasure. The samples were transported in carry-on luggage that accompanied Mr. Kavowras and were stored in his office in a secure location.

[373] Merck presented Ms. Giuliani to speak to the delivery chain from the hands of Mr. Kavowras to Dr. Davies. The samples were delivered to Ms. Giuliani who stored them in the company vault, and arranged for their delivery to Dr. Davies. Dr. Davies testified that the samples he received were in “perfect” condition.

[374] The evidence presented by Merck shows that the chain of evidence was intact and that the samples delivered to Dr. Davies were in an unaltered form.

[375] Apotex does not take issue with the transmittal of the samples to Dr. Davies. However, the problem is that these samples were taken from Blue Treasure between 2000 and 2001. There is no clear evidence that these samples were samples of the Blue Treasure lovastatin manufactured during the relevant time period from 1997 to 1999. Merck has failed to persuade me that the samples are representative of the lovastatin made, sold and distributed by Apotex Inc. Without the link of the samples taken by Mr. Kavowras to the lovastatin produced by Blue Treasure during the 1997 to 1999 period, I am unable to conclude that any DNA evidence from Dr. Davies can establish infringement.

[376] The situation with respect to the Apo-lovastatin tablets is different. There is no dispute that the source of the tablets tested was AFI batch CR0157. Thus, if I conclude, on a balance of probabilities, that the CR0157 tablets tested in the Davies Lab contained the DNA of *Aspergillus terreus* that was not the result of contamination of the samples, infringement has been demonstrated.

[377] Moreover, if I am wrong in my conclusion with respect to the lack of nexus in the Blue Treasure samples, the question before me would be whether the evidence establishes that those Blue Treasure samples contained the DNA of *Aspergillus terreus* that was not, on a balance of probabilities, the result of contamination. If it does, infringement has been demonstrated.

C. *Reproducibility of the testing in the Davies Lab*

[378] Apotex argues that I should reject the testing done in the Davies Lab because Dr. Poinar was unable to reproduce his results.

[379] In addition to being asked to provide his opinion on Dr. Davies's work, Dr. Poinar was retained by counsel for Apotex to design and carry out experiments with the same materials that were tested in the Davies Lab. Dr. Poinar tested 12 lovastatin samples made by AFI or Blue Treasure. For control purposes, Dr. Poinar's experiments included lovastatin samples that were known to have been produced with *Aspergillus terreus.* According to Apotex, Dr. Poinar used an extraction method that was essentially the same as Dr. Davies's protocol. Dr. Poinar concluded that: "both *A. terreus* and *C. fuckelii* DNA were absent in all samples tested". By way of

apparent explanation, Dr. Poinar observed that (Poinar Expert Report, Exhibit 135, p.15 "conclusion"):

> The sample processing and/or extraction steps are too lossful to permit detection of trace amounts of DNA from the source fungus (neither *A. terreus* or *C.fuckelii* was detected in samples of known origin).

[380] In other words, Dr. Poinar concluded that it is impossible to obtain detectable amounts of DNA from pharmaceutical fungal products using the experimental methods employed by Dr. Davies.

[381] Apotex relies on the evidence of Dr. Poinar to draw the conclusion that any positive results observed by Dr. Davies were as a result of contamination, not endogenous DNA.

[382] It appears that Dr. Poinar approached his experiments with the opinion that it is unlikely that DNA would survive (Poinar Expert Report, Exhibit 135, para. 62):

> … a careful examination of the entire procedure for the fermentation, extraction, recrystalization and purification of lovastatin makes it unlikely that DNA would survive this procedure.

During his oral testimony, he restated this view:

> So it is surprising, although certainly not impossible, that DNA would actually then survive that.

[383] Given Dr. Poinar's initial starting bias, is there any doubt that his experiments would fail to find DNA? It appears to me that there is a real risk that Dr. Poinar brought a confirmational bias to his laboratory work. In other words, I question whether Dr. Poinar carried out the

experiments to confirm his thesis that DNA would not be present, rather than with an open, independent mind.

[384] Even putting aside my concern about Dr. Poinar's approach to the experiments, I have serious problems with his experimental methods and results.

[385] The first concern relates to Dr. Poinar's experiences with the *Aspergillus terreus* assay. On this issue, Dr. Gilbert, accepted as an expert in the area of microbial genetics and microbiology, was of great assistance to the Court. During cross-examination, Dr. Gilbert was shown certain of the data from Dr. Poinar's experiments. In particular, he was shown two sets of qPCR data. Without knowing (as we do now) whether the information came from the *Coniothyrium fuckelii* assay or the *Aspergillus terreus* assay, he was asked to comment on various aspects of those data. The first series of slides consisted of data from the *Coniothyrium fuckelii* assay. Dr. Gilbert described the various melting curves as "very good-looking" and "pretty nice". With respect to the *Coniothyrium fuckelii* series of slides, he agreed that the data reflected an "experiment in which the PCR reactions [are] well behaved and as expected" and that the reaction was "running well". Dr. Gilbert acknowledged that the standard curve for the *Coniothyrium fuckelii* assay was typical of "a PCR reaction that is running well and predicatively as expected". The gel samples shown to Dr. Gilbert were described as "pretty much a textbook example".

[386] The situation changed dramatically when Dr. Gilbert was shown the *Aspergillus terreus* data. For example, whereas the efficiency for one of the *Coniothyrium fuckelii* slides was

described as 93.5%, the efficiency of a standard curve for an *Aspergillus terreus* assay was only 70%. Dr. Gilbert opined that the experimenter was “having problems with his quantification” and that “possibly”, he was having problems with the primers, reactants or inhibition, problems that were not apparent in the *Coniothyrium fuckelii* assay.

[387] Overall, Dr. Gilbert agreed that, even apart from quantification, the stochasticity, randomness and unexpected results were an indication that the *A. terreus* experiment did not run as well or as smoothly as the *Coniothyrium fuckelii* assay. He also acknowledged that the data supported this conclusion.

[388] The necessary corollary of Dr. Gilbert’s opinion is that Dr. Poinar’s results are reliable regarding the absence of *C. fuckelii* but that they cannot be used as a basis to rule out the presence of *A. terreus*.

[389] The next problem with Dr. Poinar’s work is that he did not employ the same methods that were carried out in the Davies Lab. Using a single round of PCR, Dr. Poinar was unable to get any hits with the *A. terreus* primers at the 0.1 copy level. However, he was able to get a hit using Dr. Davies’s nested PCR reaction. Despite the possibility that it would confirm Dr. Davies’s results and despite success at the 0.1 copy level with Dr. Davies’s protocol, Dr. Poinar did not attempt to reproduce or run a single sample through Dr. Davies’s entire nested PCR protocol. Finally, Dr. Poinar agreed with the following premise put to him in cross-examination:

> Q. You can't, based on your experiments, rule out the possibility that if you had done his experiment, reproduced his experiment, you might have found terreus?

A. No.

[390] Based on the evidence before me, I cannot conclude that Dr. Davies's work is not reproducible.

D. *Failure of Dr. Davies to find C. fuckelii DNA in the tablets from batch CR0157*

[391] As noted above, Dr. Davies found *A. terreus* DNA in the tablets from AFI batch CR0157 but did not find any *C. fuckelii* DNA in the tablets. On its face, this appears to be inconsistent with Merck's theory that batch CR0157 was likely a mix of *Coniothyrium fuckelii* lovastatin and *Aspergillus terreus* lovastatin. In final argument, Apotex stated that this alleged inconsistency "is fundamentally fatal to any reliance upon the Davies [Lab] testing", and described its position as follows:

> [Dr. Davies] did not find CF when he should have, but he found AT when he should not have. The AT could only, in that scenario, have been exogenous AT.
> ....
>
> The other alternative on CR0157 is that it is a mixture. Some AT lovastatin was thrown into the mix, but much of it, most of it, I believe, even on that scenario, was CF lovastatin.
>
> So on that scenario, it contains both CF and AT lovastatin. Dr. Davies should have detected AT and he should have detected CF. He still didn't detect CF under that scenario, which calls into question his testing and calls into question whether the DNA survives, and indicates that the AT that he did find, again, must be exogenous DNA, because he didn't find the CF.

[392] The position of Apotex is based on what I believe is an incorrect assumption. A failure to find a particular micro-organism through DNA testing is not determinative that the micro-organism is not present. On the other hand, assuming appropriate laboratory procedures and no contamination, a finding of a specific micro-organism is strong evidence that the micro-organism is present in the sample. This was acknowledged by Dr. Poinar during his cross-examination:

> Q. . . . If you want to say to someone, Look, in my opinion, DNA is absent from this sample, the actual -- the scientifically correct proposition is, always, DNA is absent from this sample to a state of detection limit; correct?
>
> A. That's correct.
>
> Q. But the flip side of the coin for the positive finding, it is not the same in science. In science you can say, I found terreus in this sample. I don't know how much was there, but I amplified it?
>
> A. Hmm hmm.
>
> Q. So to that extent, the positive finding is different from what you need to prove the negative?
>
> A. As long as all the proper precautions are put into place. So had all of the extraction controls and PCR controls been there, then the possibility would exist; that's correct.

[393] For example, we know that Dr. Poinar did not find any *A. terreus* DNA in any of the samples that he tested. Yet, we also know that there were lovastatin samples provided to Dr. Poinar – in addition to the samples in issue – that clearly contained *Aspergillus terreus* DNA. Nevertheless, Dr. Poinar was unable to confirm the presence of this micro-organism. As discussed above, I have rejected Dr. Poinar's presumption that DNA cannot be found in such samples. It follows that his conclusion that *Aspergillus terreus* DNA was not present in the

samples is incorrect; *Aspergillus terreus* DNA was present and Dr. Poinar simply did not use adequate experimental methods to find the DNA.

[394] Applying this analysis to Dr. Davies, I conclude that the failure of Dr. Davies to find *Coniothyrium fuckelii*, even if it existed in batch CR0157, does not mean his finding with respect to *Aspergillus terreus* cannot be relied on. It certainly does not follow, as asserted by Apotex, that the DNA found by Dr. Davies in AFI batch CR0157 must be exogenous.

[395] A large caveat must be introduced at this point. I have rejected Apotex's reliance on either Dr. Poinar's inability to find *Coniothyrium fuckelii* or *Aspergillus terreus* or Dr. Davies's failure to find *Coniothyrium fuckelii* DNA in the CR0157 tablets. However, that does not necessarily mean that I will accept Dr. Davies's conclusions. As stated by Dr. Poinar, "all the proper precautions" must be in place before one can rely on the results of the DNA testing. That brings me to the key issue with respect to the DNA evidence relied on by Merck: Is the DNA evidence reliable? Stated differently, were "proper precautions" used in the Davies Lab? Any discussion of this question must begin with the opinions of the experts put forward by the Defendants in response to Dr. Davies's DNA evidence.

E. *DNA evidence and the Apotex Experts*

[396] Apotex's response to the DNA evidence rests on the criticisms of Dr. Davies's work provided by three experts – Drs. Gilbert, Poinar and Taylor.

[397] Dr. Taylor was qualified to provide opinions to the Court as an expert mycologist, and microbiologist with particular expertise in fungal DNA evolution and fungal DNA PCR amplifications. Dr. Taylor opined on Dr. Davies's Expert Report and DNA testing results, particularly with respect to the possibility of contamination in the Davies Lab.

[398] Dr. Gilbert was qualified as an expert in the analysis of low copy and degraded DNA. His expert testimony and report deal with the issue of infringement. He explains the problems with the use of ancient or degraded DNA (referred to as ancient DNA). Dr. Gilbert was asked to examine Dr. Davies's laboratory notebooks, and comment on whether the conclusions generated were justified by the methods used.

[399] Dr. Poinar was qualified as an expert in the extraction and characterization of low copy and degraded DNA. Dr. Poinar reviewed the experiments performed by the Davies Lab, and (discussed above) attempted to replicate the results through testing of his own. Dr. Poinar was asked to answer two general questions: first, whether or not the experimental design of Dr. Davies matched the rigour necessary for an ancient DNA or low template sample project; second, whether Dr. Davies's data support his hypothesis that *Aspergillus terreus* DNA was found in samples of lovastatin from the Defendants.

[400] As a general rule of evidence, witnesses may not give opinion evidence, but may only testify as to the matters within their knowledge, observation and experience. An exception to this rule applies to expert witnesses. Experts are necessary to assist the Court in scientific matters that would not normally be within the knowledge of the judge. However, before accepting the

opinion evidence, the trier of fact must determine the admissibility of the evidence in accordance with four criteria: relevance, necessity in assisting the trier of fact, the absence of an exclusionary rule and a properly qualified expert (*R v. Mohan,* [1994] 2 S.C.R. 9, 114 D.L.R. (4th) 419).

[401] In this case, Drs. Taylor, Gilbert and Poinar appear to satisfy three of the four criteria. However, given the narrowness of their experience and the focus of their opinions on ancient DNA, I seriously question the relevance of their opinions. This is true for all three experts, although more so with respect to Dr. Poinar and Dr. Gilbert. While the level of my concern does not lead me to conclude that all of their opinion evidence is inadmissible, it does reflect on the weight that should be given to their opinions. The key problem exists with the characterization of the DNA tested by Dr. Davies as ancient DNA.

(1) What is Ancient DNA?

[402] The first question is: what is ancient DNA? On the record before me, there is no clear definition of this term. However, each of the Defendants' experts provided insights on how to understand what ancient DNA is:

- Dr. Poinar stated that (Poinar Expert Report, Exhibit 135, para. 2):

  > The study of ancient DNA is the retrieval and meticulous characterization of DNA sequences from samples which are assumed to be heavily degraded, in low copy numbers and typically stemming from forensic, fossil, sub-fossil, archeological, and palenontological remains.

- Dr. Gilbert stated that (Gilbert Expert Report, Exhibit 130, para. 8):

  > I have been involved in the analysis of a range of materials that contain degraded DNA, and/or low copy number modern DNA. These include ancient bone and tooth material, often dating back tens of thousands of years in age, hair shaft and root, nail, horn, skin (both tanned into leather and dried), mummified soft tissues, feather, eggshell, ancient plant seeds and leaves, formalin and Bouin's solution fixed soft tissues, historic blood samples, feces, urine, soil, ice and honey.

- Dr. Taylor stated that (Taylor Expert Report, Exhibit 124, para. 25) :

  > This scarcity of DNA in the lovastatin samples makes analysis of DNA from these samples akin to analysis of DNA from archeological samples, the field of research referred to above as "ancient DNA". A key complication of ancient DNA research is the high likelihood of contamination of the sample with DNA from modern sources of by DNA that has been amplified by PCR from modern DNA, unless the necessary precautions are taken.

[403] There is a clear gap in these opinions – they fail to provide a comprehensive analysis of how DNA was degraded in the process of making a pharmaceutical product, or even how to compare the DNA in ancient DNA to DNA derived from a pharmaceutical product. Without this evidence, I am unable to compare the evidence presented on ancient DNA to evidence presented by Dr. Davies.

[404] Dr. Taylor made a sweeping statement in his report that "the scarcity of DNA … is akin to archaeological samples". In the absence of a comprehensive analysis, this is neither a convincing statement nor a scientific one. What is the basis for his knowledge that the DNA in lovastatin is scarce? Where is the evidence that shows us that these two types of DNA can be

considered analogous? Without something further, I do not see how it can be logical to compare the level of DNA available from ancient bone and tooth material to DNA derived from a pharmaceutical product.

(2) Is DNA derived from a pharmaceutical product degraded or fragmented?

[405] The next step is to consider the condition or state of DNA derived from a pharmaceutical product. During the trial, there was some controversy over the semantics of whether the DNA derived from the lovastatin samples, and tested by Dr. Davies, was “fragmented” or “degraded”. Apotex argues that Dr. Davies specifically described the DNA that was the subject of his experiments as “degraded DNA”. Although this is correct, Dr. Davies provided a sufficient explanation of what was meant by the use of this term in his Expert Report.

[406] During his oral testimony, Dr. Davies described the process whereby the fungal DNA in lovastatin is fragmented during industrial processing. He explained that DNA is released by the cells which expose the DNA to shearing forces in the fermentation machine. This was not contested. The issue was whether these shearing forces would cause “fragmentation” or “degradation”. Dr. Davies was asked about this during cross-examination:

> Q. You just told me a few moments ago that there would be fragments or, the word that you didn't like to use, degradation; would I be right that you would agree with this, that although some of the DNA survives in the pharmaceutical process involved here, there, unquestionably, would be some DNA that would be degraded during the process?
>
> A. In the case of a fermentation process, I think I mentioned this before, during fermentation and particularly at the end, cells begin to LYSE, they break and they release DNA. That DNA is

> going to be sheared; it's going to be exposed to shearing forces of the big stirrers that are used in the fermentation. And shearing will break DNA.
>
> For one thing, Aspergillus DNA often has a lot of protein bound to it which might stabilize it, but we planned our experiments with the expectation that the DNA was going to be sheared. It would never shear down to almost nothing.

[407] In his report, Dr. Davies uses the word “degraded” when referring to the DNA which was the subject of his experiments. However, during oral testimony, Dr. Davies clarified that he equates the word “degraded” to “fragmented” – which is the word he should have used in his Expert Report. Dr. Davies explained that fragmentation is a normal process that occurs to all DNA which is outside a cell. He did not intentionally refer to “degradation” as synonymous with the process that results in ancient DNA.

> Q. You talk about the difficulties your lab experienced, you say:"I underscored the difficulty in obtaining DNA from pharmaceutical samples."And then you should read it, but go to the sentence that begins, "although some DNA survives the process."
>
> A. Yes.
>
> Q. It says:
>
> "There is unquestionably some DNA that is degraded during the process."Do you accept that as correct, that's your view?
>
> A. I do.
>
> THE COURT: Is that because you equate the word degraded with fragmented?
>
> THE WITNESS: Yes. This is different.
>
> THE COURT: Let me get here to paragraph 63. When you use the word "degraded" in paragraph 63, do you mean fragmented?
>
> THE WITNESS: I mean a very general process.

> THE COURT: Is there something beside fragmentation that you mean by the word degraded in that paragraph?
>
> THE WITNESS: Yes, Your Honour. There are enzymes, chemicals, in the reaction in the fermenter that could chemically modify the DNA.

[408] Dr. Davies goes on to opine that there is no clear evidence that the *A. terreus* DNA is "degraded" (in terms of the ancient DNA reference) during the fermentation process.

> Q. Going back to my question, do you not agree with this, that a though some DNA survives the fermentation, purification process, that there, unquestionably, would be some DNA that is degraded during the process?
>
> A. If we buy degradation, we're talking about chemical reactions, and I would say yes, it's possible.
>
> Q. Not unquestionable?
>
> A. I don't know, you see. Nobody's ever looked. You've got a fermenter with things DNA has never seen and you're stirring it up.I don't know anybody is going to look to see what the DNA would be like and how it was broken. We didn't look at the fermenter. We only looked at the powder.

[409] In my view, Dr. Davies's explanation is clear as to why DNA derived from a pharmaceutical process could be considered to be "fragmented" but not "degraded".

[410] So, what does this mean to me? Apotex's experts assume that the DNA tested by the Davies Lab was "degraded" in the same manner that ancient DNA is degraded. I do not agree. The only relevant evidence presented before me on this issue was that of Dr. Davies. I conclude that the DNA tested by Dr. Daves is considered to be "fragmented" but not "degraded".

(3) Can one compare how DNA derived from a pharmaceutical product is fragmented to how DNA from “ancient DNA” is degraded?

[411] After considering the evidence on what is ancient DNA, I will now consider whether DNA derived from a pharmaceutical product that is “fragmented” can accurately be referred to as ancient DNA. I conclude that it cannot.

[412] In my view, it does not logically flow to compare DNA from “ancient bone and tooth material, often dating back tens of thousands of years” to DNA from *Aspergillus terreus* which has been processed into a pharmaceutical product. This is true especially in light of understanding that the subject DNA is not “degraded” in the same manner.

[413] Without specific expert evidence on this, it is not logical to compare the two. The Defendants’ experts provide no relevant evidence on this point. However, Dr. Davies explicitly states that one cannot compare ancient DNA to DNA derived by a pharmaceutical process.

> Q. Tell me what you understand the words "ancient DNA" to mean to at least those that use the expression?”
>
> A. As I understand it, it is DNA being isolated from remnants of earlier civilization, animals, from earlier stages, things of that type, and looking for DNA from those samples and trying to identify them. So the sequencing of some old human genomes recently. I don't know if that's called ancient DNA or not.
>
> Q. In your description of it, would I be correct that the DNA one has in the context that you've given me for in ancient DNA, is DNA that is either low copy number DNA or degraded DNA?
>
> A. Depends how you define degraded.
>
> Q. How would you define degraded?

A. I think there are two kinds of degradation.

Q. What are they?

A. One is that the DNA can be broken to give very low molecular weight fragments which makes it more difficult to do a PCR.

. . .

Q. On the last sentence, the process of cleaving that you talked about in that sentence, that causes, according to your sentence, further degradation, not a new but further suggestion that the earlier process that you described, the purification steps earlier, causes degradation, and that leads to further degradation through the cleavage from the enzymes, correct?

A. That is correct. What I should have said is that the DNA is really modified and broken up in a horrible way, and there would be very little intact chromosomal DNA but there would be fragments, and some of those would not work in PCR because they'd be modified further. That's the difference between this and ancient DNA, and things like that.

Q. I don't know what you mean by that. What do you mean by ancient DNA?

A. It's DNA from million year old remains and things of this type.

Q. You're suggesting that that DNA is not fragmented and not degraded and not broken up?

A. It's everything. It's even worse. So the techniques used for ancient DNA are really very specific, and it's not the same as this.

Q. Because it's even more extreme and ancient DNA versus what you encountered here?

A.Yes, cosmic rays have been acting on it for a long time. But as I think I mentioned right at the beginning, one of the biggest problems with what they call ancient DNA is the question of desiccation, and desiccation causes quite severe damage to DNA.

[Emphasis added.]

[414] Dr. Davies provides his expert opinion that DNA that has been hit with cosmic rays for thousands of years – DNA that scientists did not think even existed until a few short years ago – cannot be compared with DNA that has been processed into a pharmaceutical product. I agree with him.

(4) Are the opinions of the Defendants' experts relevant to fragmented DNA from pharmaceutical products?

[415] Having concluded that ancient DNA is not comparable to DNA derived from a pharmaceutical product, I turn to a consideration of whether the opinions presented by the Defendants' experts extend beyond the field of ancient DNA. In other words, can the opinions of any of the experts assist the Court in gaining a different understanding of the DNA testing from fungal pharmaceutical compounds than what was provided by Dr. Davies?

[416] In my view, none of the experts has provided me with the necessary link between ancient DNA and the DNA in issue. Apotex has failed to satisfy me that the evidence of these experts is relevant to the issues before me.

[417] Dr. Waldo Taylor was the only expert (other than Dr. Davies) whose expertise extended beyond the field of ancient DNA. During his examination-in-chief, he stated the following:

> Q. I just want to ask you about the expression "ancient DNA". Can you describe what you understand that to mean?
>
> A. Sure. As I mentioned, when the PCR reaction became available it was possible to examine DNA and biological specimens, or really any specimen, where DNA was wanting, where it was scarce. So that field has grown and it encompasses people who study ancient DNA, who study DNA that survives in

> the fossil specimens, things like Neanderthal bones or organisms in amber. It includes forensic studies where there's a little amount of DNA associated with some social interaction that you'd like to study. It includes the study that we're concerned with today, trying to identify the organism that produced a pharmaceutical compound.
>
> [Emphasis added.]

[418] However, during his cross-examination Dr. Taylor acknowledged that he was not fully aware of "the whole story" of how the lovastatin samples tested in the Davies Lab were treated or prepared.

[419] Dr. Taylor's opinions are seriously undermined by his admission that he lacks understanding of how the relevant pharmaceutical compounds have been prepared or treated. It is inadequate for an expert to explicitly state that the subject DNA is comparable to ancient DNA when he does not know the scientific basis for this comparison.

[420] Neither Dr. Gilbert nor Dr. Poinar offered their opinions on how, if at all, fragmented DNA from a pharmaceutical compound could be treated as ancient DNA.

[421] According to Dr. Gilbert, there are millions of scientists in the world who have access to, use or rely upon PCR data; yet, there were only a "handful of people on the earth" who are qualified to undertake the kind of ancient DNA analysis Apotex promotes. It would have been more helpful to the Court (and relevant to the issues of this case) if Apotex had presented DNA experts who operated outside this "handful of people on the earth".

[422] In sum, I have difficulty with the opinions of the Apotex experts. Their opinions are based on an assumption that Dr. Davies's work and opinion could be evaluated against the same standards, protocols and norms as would be used by the "handful of people on the earth" with an expertise in ancient DNA. I am not satisfied that this assumption is correct. This problem informs my evaluation of the criticisms levelled at Dr. Davies's work. The Apotex experts are providing their opinions through a very narrow prism that is only marginally relevant – at best – to the issues before me.

F. *Contamination*

[423] As we know, Dr. Davies had 13 hits for *Aspergillus terreus* DNA from three different samples. In their arguments, the Defendants raise many, many problems with Dr. Davies's opinion, his testimony at the trial and the procedures and results from the Davies Lab. I have considered all of their concerns. The most serious allegation is the risk that the *Aspergillus terreus* DNA found in the samples tested was the result of contamination by exogenous *Aspergillus terreus*. In other words, the Defendants submit that the risk of contamination in the Davies Lab was so high that I cannot accept the DNA testing evidence of Dr. Davies as reliable.

[424] As all of the experts would agree, contamination is always a serious risk in DNA testing. I acknowledge the risk. The question for this Court is whether the risk of contamination makes it more likely than not that Dr. Davies's *Aspergillus terreus* DNA findings are false.

(1) Dr. Davies

[425] Dr. Davies was clearly aware of the risk of contamination. Dr. Davies addressed the issue of laboratory contamination on several occasions during his testimony and in his Expert Report. Dr. Davies stated (Davies Expert Report, Exhibit 55, para. 77):

> I do not consider contamination to be a likely explanation to account for the presence of *Aspergillus terreus*. For example, if our laboratory was contaminated, I would have expected to see *Aspergillus terreus* amplicons in the negative controls. However, this was not the case.

[426] Dr. Davies cautioned that there is always a possibility of a contamination while carrying out a PCR reaction with DNA. However, during his oral testimony, he insisted that, "[the Davies Lab] took every possibility to avoid contamination. We're not forensic scientists, but we can work clean."

[427] Dr. Davies likened the scenario of contamination in the subject experiments to "the chance that lightening would hit you." He explained that his two investigators, Grace Yim and Karen Lu, were extremely careful workers and precautions were taken to prevent contamination, including:

- working in a sterilized area to kill bacteria and fungi that could be a source of contamination;

- autoclaving the micro-pipets and tips to sterilize and prevent cross-experiment contamination;

- operating in a UV-radiated, stainless steel biosafety hood to purify the incoming air and allow for easy cleaning of the hood; and

- utilizing experiments with zero DNA controls, and following the protocol that the experiment would be repeated if contamination was found in the zero DNA control.

[428] Dr. Davies was convinced that contamination was not responsible for the results of these experiments. He opined that the fact that the Davies Lab never found *Coniothyrium fuckelii* or any other fugus of the genus *Aspergillus* (other than *terreus*) as a contaminant, was evidence to support his assertion that contamination was not responsible. Dr. Davies observed that it was hard to believe that, if contamination had been present in the experiments, it would only be found in the form of *Aspergillus terreus*.

[429] Lastly, as Dr. Davies most poignantly stated, “DNA doesn’t fly” or “float around in the air”.

[430] Against the backdrop of Dr. Davies’s expert testimony, I turn to the evidence of the experts produced by Apotex. In general, as discussed above, the Apotex experts brought a very narrow perspective to the question of contamination. All three imposed incredibly high standards on the work of DNA laboratories and began with the assumption that Dr. Davies was dealing with DNA that was akin to ancient DNA that might be found in the 1000-year old remains of extinct animals. Quite simply, these experts imposed an overall standard on the DNA testing

performed by the Davies Lab that is not reasonable in the circumstances. Two experts – Dr. Taylor and Dr. Gilbert – were particularly stubborn in their opinions on contamination in the Davies Lab.

(2) Dr. Taylor

[431] Dr. Taylor equated the analysis of the tested lovastatin to an "analysis of DNA from archaeological samples" (Taylor Expert Report, Exhibit 124, para. 25). For the reasons expressed earlier, I am of the view that this assumption is flawed, or unsupported by the record.

[432] Directly following from this assumption, Dr. Taylor expressed the view that a "substantial risk of contamination" could come from two sources: (a) cultures of *Aspergillus terreus* which were used by Merck to produce lovastatin; or, (b) *Aspergillus terreus* DNA that was PCR amplified in the Davies Lab.

[433] Dr. Taylor concluded that (Taylor Expert Report, Exhibit 124, para. 28):

> If Dr. Davies did in fact detect *Aspergillus terreus* DNA, then his own laboratory practices very likely caused his samples to become contaminated with such DNA from *Aspergillus terreus* cultures or from DNA that been PCR amplified from *Aspergillus terreus* DNA.

[434] During cross-examination, Dr. Taylor stated that the most likely source of contamination was *Aspergillus terreus* DNA from PCR amplifications in the Davies Lab. This theory was discussed with Dr. Gilbert during cross-examination. Dr. Gilbert explained why the amplified material posed more of a risk; it is because the "PCR part" would "be more concentrated" with

DNA. However, as the evidence shows, the strains of both *Aspergillus terreus* and *Coniothyrium fuckelii* were present in the Davies Lab at the relevant time. Dr. Gilbert also confirmed that the risk of contamination from the control DNA from *Aspergillus terreus* or *Coniothyrium fuckelii* was equivalent, even though the DNA concentration would differ. Yet, Dr. Davies found *Aspergillus terreus* DNA in 13 experiments but never documented a single instance of *Coniothyrium fuckelii*. How could it be that amplified *Aspergillus terreus* DNA would cause contamination but not the *Coniothyrium fuckelii* DNA? Dr. Gilbert repeatedly refused to accept the possibility that zero findings of *Coniothyrium fuckelii* DNA should reassure the experimenter that contamination by *Aspergillus terreus* was not probable. I find his denials to be unhelpful and, frankly, illogical. Thus, Merck submits, Dr. Taylor's theory does not withstand examination. I agree. Zero findings of *Coniothyrium fuckelii* demonstrates the weakness in the theory that contamination would, more likely than not, occur from *Aspergillus terreus* DNA that was amplified by PCR in the Davies Lab.

[435] Another theory of contamination presented by Dr. Taylor was the possibility of airborne spores. I do not accept this as likely in the Davies Lab. The use of a biosafety hood with purified air would dramatically reduce the possibility of such contamination. Further, Dr. Taylor acknowledged that he had never studied the ability to amplify from a single spore of *Aspergillus terreus* and admitted that it was speculative to conclude that a single spore would amplify by PCR.

[436] A final concern of Dr. Taylor relates to his reading of the various “gels” that recorded the experimental results. Dr. Taylor noted a “milestone” on the gels. Dr. Taylor observed the following (Taylor Expert Report, Exhibit 124, para. 33):

> . . . Dr. Davies’ laboratory records from 2007 confirm that DNA was amplified from the lovastatin samples using coniothyrium fuckelii specific primers, thus indicating the presence of coniothyrium fuckelii DNA in the sample. However, Dr. Davies did not mention this in his affidavit. Accordingly, Dr. Davies’ failure to acknowledge coniothyrium fuckelii as the potential source organism, based on his erroneous assertion that no coniothyrium fuckelii DNA was found, was not warranted.

[437] In other words, Dr. Taylor was of the opinion that Dr. Davies had positive findings of *Coniothyrium fuckelii* that were overlooked or never reported. I agree that an unreported instance of *Coniothyrium fuckelii* would be a critical contention with respect to the possibility of contamination and also with respect to Dr. Davies’s conclusion that there was no *Coniothyrium fuckelii* DNA found in any of the samples tested. However, examination of Dr. Taylor’s statement and observations by Dr. Gilbert and Dr. Poinar diminish the significance of this observation.

[438] During his cross-examination, Dr. Taylor acknowledged that his conclusion that this was *Coniothyrium fuckelii* was speculative; he agreed that the first amplification of DNA using a *C. fuckelii* primer may have been *Coniothyrium fuckelii* DNA or “may be OJ Simpson’s DNA”. Dr. Poinar agreed that, based on the data, one could not conclude that the band observed by Dr. Taylor was a band of *Coniothyrium fuckelii* DNA. When Dr. Gilbert was asked about the existence of any bands that were the correct size for *Coniothyrium fuckelii* using the *Coniothyrium fuckelii* specific primers, Dr. Gilbert responded that there were “zero” such bands.

[439] Viewed as a whole, I do not find that Dr. Taylor's opinions regarding contamination are supported by the record.

(3) Dr. Gilbert

[440] Dr. Gilbert provided his expert opinion that "contamination presents a serious challenge to the data generated by Dr. Davies's team". I do not believe that anyone would disagree with this statement. However, Dr. Gilbert continues to express his view that, "as a result, his results cannot be viewed as reliable."

[441] The first problem that I have with Dr. Gilbert's opinion is that it is directed to his field of specialization – the fields of ancient DNA and forensic genetics. In his Expert Report, Dr. Gilbert refers to samples that "were millions of years old". His entire opinion is premised on the assumption – unexplained, in my view – that Dr. Davies was working with degraded DNA that was comparable to ancient DNA. As discussed above, I am not persuaded that this is a meaningful comparison.

[442] Moreover, the contamination theory posited by Dr. Gilbert (and Drs. Taylor and Poinar) is that exogenous *Aspergillus terreus* resulted in the positive findings by the Davies Lab. Thus, unless the experts can identify a credible source of the exogenous *Aspergillus terreus* DNA, the theory does not stand up to scrutiny. Upon cross-examination, Dr. Gilbert acknowledged that there was no evidence that contaminants, if they existed in the Davies Lab, were *Aspergillus terreus*.

[443] Further, how has Dr. Gilbert measured or defined the term “reliable”? Can the possibility of contamination explain away every one of the 13 “hits”? Does the risk of contamination make it more likely than not that *Aspergillus terreus* does not exist in the samples? Or, is contamination merely a possibly?

[444] In sum, I am not persuaded that the risk of contamination in the Davies Lab rises to the level where, on a balance of probabilities, I cannot rely on the results obtained and opined on by Dr. Davies.

G. *Other criticisms of Dr. Davies’s opinion*

[445] The Defendants levelled a number of other criticisms at the work of Dr. Davies. Specifically, the Defendants submit that the following principles must be followed to determine whether the Court should ignore the expert evidence of Dr. Davies:

- Where an expert’s conclusion is not appropriately explained and supported, it may properly be given no weight by the trier of fact (*Backman v. Canada* (1999), 178 D.L.R. (4th) 126 at para. 34, 246 N.R. 309 (F.C.A.)).

- Likewise, for a Court to accept an expert’s opinion, the trier of fact must know the facts and/or assumptions upon which the expert has based his or her opinion (*Johnson & Johnson v. William H. Rorer, (Canada) Ltd.* (1980), 48 C.P.R. (2d) 58 at para. 7, [1980] F.C.J. No. 200 (QL) (F.C.T.D.)).

- Where those facts turn out to be inaccurate or incomplete, the weight given to an expert's opinion may be significantly reduced (*Misik (E.) v. M.N.R.*, [1993] 1 C.T.C. 2360 at p. 2373, [1993] T.C.J. No. 13 (QL) (T.C.C.)).

[446] In support of their position that the opinion of Dr. Davies should be rejected, the Defendants point to "spurious bands" seen on some of the "gels". These bands, in the view of the Defendants, demonstrate that Dr. Davies's opinion was inaccurate.

[447] In principle, I agree with the Defendant's argument that an expert should: (1) appropriately explain their conclusions; (2) inform the Court of the underlying facts and/or assumptions; and (3) provide accurate and complete information. If unable to do so, it should be expected that the weight of their opinion will be significantly reduced.

[448] However, I believe that the Defendants are misapplying these principles to the opinions given by Dr. Davies.

(1) Lack of knowledge

[449] I agree with the Defendants that there were aspects of the experiments performed in the Davies Lab that Dr. Davies was unable to describe to the Court. However, the critical question is whether his knowledge of the technical aspects of the experiments was fundamental to his expert opinion. I do not think it was.

[450] If one accepts that someone is an expert in their field (as the Defendants did in the case of Dr. Davies), the parties must provide the Court with a clear understanding of what their expertise is. A problem arose in this case because of a misunderstanding between what constitutes being an expert in the science of microbiology and an expert in performing the technical experiments of microbiology. There obviously was confusion of what was expected of Dr. Davies. Dr. Davies obtained his Ph.D in 1956, and reached professor emeritus status in 1997. He is unquestionably an expert in his field. One does not rise to that level at a Canadian university without having outstanding accomplishments in an area of expertise. However, it is not surprising that someone like Dr. Davies, who is in charge of a laboratory with many students and technicians, is not personally performing the experiments and may not be knowledgeable on all of the technical aspects of the experimental procedure. Obviously (and somewhat critically of Dr. Davies), I am of the view that Dr. Davies should have prepared better for his testimony. However, unless the lack of knowledge goes the heart and substance of Dr. Davies's opinion, I would not be persuaded to reject that opinion.

[451] The Defendants agreed, after reviewing his Expert Report, and before his oral testimony, that Dr. Davies was an expert in microbiology and microbial genetics. That expertise includes the use of DNA techniques for studying microbes. That expertise – and not the minutia of laboratory procedures – was the focus of his opinion. I do not agree with the Defendants that Dr. Davies's lack of knowledge of some the technical aspects of the experiments should necessarily lead this Court to the conclusion that the evidence is unreliable.

(2) Incomplete Report & Lack of Disclosure

[452] The Defendants argue that Dr. Davies was incorrect and incomplete in his report of, and conclusions as to, the majority of the experiments disclosed. I agree that Dr. Davies's notebooks and conclusions were incomplete. However, the determinative question is whether the missing information is fundamental to his expert opinion. I do not believe it was.

[453] The Defendants refer to the following incidents of incompleteness:

- In 2003, experiments 13, 19 and 20 are disclosed. The inference is that at least 17 other experiments were not disclosed. Thus, 17 of 20 or 85% of all experiments were not disclosed.

- In Karen Lu's 2007 work, experiments 7, 8, 18, 20, 22, 23 and 24 are disclosed. The inference is that at least 17 other experiments were not disclosed. Thus, 17 of 24 or approximately 71% of all experiments were not disclosed.
- In Grace Yim's 2007 work, experiments 32, 33, 35 and 36 are disclosed. The inference is that at least 8 other experiments are not disclosed. Thus, 8 of 12 or approximately 67% of all experiments were not disclosed.

- In total, 42 or 54 experiments, or 78% of all experiments were not disclosed.

[454] The Defendants submit that Dr. Davies provided an incomplete picture of the experiments performed by only providing selected pages for litigation. The Defendants allege that Dr. Davies erred by providing only the pages that "would bear on the conclusion", and not all of the pages that were relevant. The Defendants further argue that Dr. Davies provided an erroneous explanation for withholding the notebook pages because "the non-disclosed experiments did not bear on the conclusion 'in any significant way'". I do not agree with the Defendants that this was an erroneous explanation.

[455] During cross-examination, Dr. Davies testified that the reason he did not disclose all of the pages relating to all of the experiments performed in his lab was that this was not "routine" procedure for a scientist. When preparing evidence to support a publication, it is "routine" for a scientist to provide only the pages that support the conclusion that the scientist has opined. There was no malice or bad faith in Dr. Davies's lack of disclosure.

> Q. You deprived a reader of coming to a different conclusion about the sufficiency or the relevance of the experiments included and not included, correct?
>
> A. No, I don't think so. May I make the point that when one publishes a scientific paper, you have to publish a logical sequence of events, and you publish the results, and you then interpret the results based on the experiments? This was not a scientific paper. Things were much simpler here than that. I believe we gave you a continuum. We selected some experiments. Some of them were experiments that didn't work that well, but you got an idea as to what was going on. I don't see anything wrong with that.

[456] During cross-examination, Dr. Davies was presented with a chart, prepared by counsel, representing the missing information. Throughout the cross-examination, I was unable to observe any missing notes or details that would have had a material impact on the overall opinion of Dr.

Davies. When asked about the chart during cross-examination, Dr. Poinar stated that all documents need to be put forward. However, he also acknowledged that, in this case, the data depicted in the chart meant little, if anything, to the conclusions being drawn by Dr. Davies.

[457] I do not agree with the Defendants that the decision of Dr. Davies to exclude certain pages must result in a conclusion that his evidence is unreliable. What is important is that the opinions of the expert not be contradicted or otherwise weakened by any missing information. By not putting forward all of the notebook pages, Dr. Davies ran the risk of not being able to substantiate his opinions. However, in this case, as admitted by Dr. Poinar, the missing information is not relevant to the overall conclusion. Accordingly, while I would have preferred that Dr. Davies had provided a more complete picture of the experiments performed, I do not consider that his opinion to be fatally flawed by his failure to do so.

(3) Unexpected results

[458] The Defendant's argue that Dr. Davies obtained unexpected results and therefore his work cannot be relied upon. At the heart of their argument is the presence of "spurious bands" that only became visible upon dramatic enlargement of a photograph of the gel that was stained and analyzed under UV light for the presence of the PCR amplified DNA

[459] The Defendants argue that the experiments of Dr. Davies were flawed because, upon investigation of the laboratory notebooks, extra bands could be seen on the gel pictures. The

Plaintiffs, on the other hand, argue that any evidence involving “photoshopped” gels should not be considered or given any weight by this Court. I agree with the Plaintiffs on this point.

[460] When presented with the greatly enlarged photographs, Dr. Davies commented that the gel photographs were manipulated by the Defendants. Dr. Davies stated:

> Your photo shopping is up to some amazing magnification … people do this to public papers sometimes and I think it’s unrealistic. It’s not what you see on the actual gel. This is not the actual gel. This is a doctored gel in my opinion … You can find many bands on PCR gels that you would not see by eye. You would not see by other detections if you photo shopped them up in some way. I am just very concerned about this, and I find it difficult to draw what I would consider to be sound conclusions

[461] I agree with Dr. Davies. The original photographs of the gels are highly technical and – frankly – confusing to this judge. How can I be certain that taking those already confusing depictions and enlarging them to this extraordinary scale does not bear a risk of introducing photographic ghosts, shadows or other images that did not originally exist? I have no evidence that such distortion of the original evidence would not introduce errors or unreliable results.

[462] Even if I were to accept that there are faint bands that were not seen in the original gels or referred to by Dr. Davies, none of this evidence accounts for Dr. Davies’s findings of *Aspergillus terreus* in the lovastatin samples.

[463] Overall, the presence of the spurious bands, or the impact of the photoshopped pictures, does not lead me to the conclusion that the results of the experiment were flawed.

IX. Infringement – Conclusion

[464] My overall conclusion is that Dr. Davies's testing results are reliable and credible evidence that the lovastatin samples tested in his laboratory contained *Aspergillus terreus* DNA. I have rejected the contamination theory of Apotex.

[465] I am satisfied that the lovastatin tablets tested originated from AFI batch CR0157. The DNA evidence satisfies me that, on a balance of probabilities, the Defendants infringed the '380 Patent with the manufacture and sale of any product from AFI batch CR0157.

[466] The situation with respect to the Blue Treasure samples is different. As noted earlier in these reasons, I am not persuaded that Merck has demonstrated a nexus between the samples tested in the Davies Lab and the allegedly infringing product. Thus, I do not accept the DNA evidence as direct evidence of infringement by the lovastatin produced by Blue Treasure. Nevertheless, the remaining evidence presented by Merck with respect to the Blue Treasure lovastatin strongly supports the conclusion that there was infringement. This is discussed earlier in these reasons. If I am wrong with respect to the lack of nexus, then I would conclude that the DNA evidence is evidence of direct infringement, a conclusion that would strengthen – but not change – my earlier finding of infringement.

X. Validity

A. *Introduction*

[467] Having determined the issues of claims construction and infringement, I now turn to the issue of validity. In their counterclaims, each of the Defendants assert that the '380 Patent is invalid. If they are correct, there will be no question of infringement; the Defendants cannot infringe an invalid patent.

[468] In an infringement action, the patentee benefits from the presumption of validity (s. 45 of the *Patent Act* and s. 43(2) of the *Patent Act* currently in force). Thus, Apotex bears the burden of proving, on a balance of probabilities, that the '380 Patent is invalid. As of the close of argument in this trial, the following remained as Apotex's grounds of invalidity:

- All of the disputed claims, except for claims 3 and 6, are invalid because they are overly broad.

- Certain of the claims are invalid because they could not demonstrate utility. In particular:

    - claims 1, 2, 5 and 13 to 15 demonstrate a lack of utility, in that not all of the compounds included in the claims are useful in fulfilling the promise of the '380 Patent; and

- the utility of the claimed subject matter, including pharmaceutical utility, demonstrates a lack of sound prediction, in that the inventor could not predict, as of the Canadian filing date, that the compounds claimed would fulfil the utility promised by the '380Patent.

- Claims 13 to 15 are invalid because of prior use or anticipation by the existence of lovastatin in a traditional Asian product known as “Red Yeast Rice”.

- The claims are invalid because Merck was not the first to invent lovastatin.

B. *Overbreadth*

[469] Apotex argues that the claims of the '380 Patent, other than claims 3 and 6, are “overbroad” because they claim processes that were not invented by the named inventors. In their submission, the invention, as claimed, comprises numerous strains or species which were not tested or evaluated by the inventors to determine, as of the priority date, whether they were capable of producing the compounds.

[470] A patent which claims more than what has been invented can be found to be invalid as being overly broad. The concept of “overbreadth” has been referred to in a number of cases before our Court. In support of its position, Apotex relies on the case of *Biovail Pharmaceuticals Inc. v. Canada (Minister of National Health and Welfare)*, 2005 FC 9, [2005] F.C.J. No. 7 (QL)

[*Biovail*]. In *Bioval*, above, at paragraph 61, Justice Harrington described the notion of "covetous claiming" as follows:

> If the inventor claims more than he should, he loses everything.
>
> > His fences must be clearly placed in order to give the necessary warning and he must not fence in any property that is not his own. [Thorsen P. in *Minerals Separation North American Corp. v. Noranda Mines Ltd*., [1947] Ex. C.R. 306 at page 52, as quoted in *Free World Trust*, supra, at para. 14]

[471] In *Biovail*, above, the patent in issue (a patent for a controlled-release pharmaceutical tablet) disclosed only one sustained-release mechanism, referred to as an osmotic process, using a compound known as HPMC as the carrier. The generic company was using a different mechanism and compound – a hydrogel process using a compound known as HPC as the carrier. Justice Harrington's key finding was that the patent was not infringed because the inventors only contemplated the osmotic process, and not the hydrogel process, which was a substantially different process. However, in the alternative, Justice Harrington considered that, if the claims were to be construed to include the hydrogel process, "the patent was invalid for covetous claiming" (*Biovail*, above, at para. 60).

[472] *Biovail*, in my view, does not support Apotex's submission on overbreadth. Unlike the patent in *Biovail*, the '380 Patent's claims and disclosure make reference to all producing species of *Aspergillus terreus*. The question of whether the inventors could extrapolate their laboratory results from the specific samples tested is a question of sound prediction and not of overbreadth.

[473] Apotex also relies on *Eli Lilly Canada Inc. v. Apotex Inc.*, 2008 FC 142, 63 C.P.R. (4th) 406 [*Eli Lilly Raloxifene (FC)*], aff'd 2009 FCA 97, 78 C.P.R. (4th) 388, a decision in respect of a patent that claimed the use of raloxifene in the treatment of osteoporosis and bone loss. At paragraphs 179-182, Justice Hughes discussed the assertion that the claims were overly broad. Key to his conclusion that the claims were overly broad was the "disconnect" between the disclosure and the claims in the patent. The disclosure limited the osteoporosis and bone loss to that without the adverse effects of estrogen therapy. In all but one of the claims in issue, there was no limitation to the use of the drug for bone loss due to estrogen-related causes. Thus, Justice Hughes concluded that all but one of the claims in issue were overly broad. The issue of overly broad claims was not overturned by the Court of Appeal.

[474] In my view, *Eli Lilly Raloxifene (FC)*, above, does not support an argument that the claims of the '380 Patent are overly broad. In the patent before me, the disclosure is consistent with the claims in issue. Contrary to the submissions of Apotex, the disclosure of the '380 Patent is not limited to the two strains of *Aspergillus terreus* that were used in the experimentation by Merck that lead to the invention.

[475] In brief, on Apotex's claim of overbreadth, I conclude that this argument, on the facts of this case, is more properly a question of sound prediction - in particular, both the factual basis for the prediction and the sufficiency of the disclosure.

C. *Utility*

(1) General Principles

[476] Apotex submits that the '380 Patent is invalid on the grounds that:

1. the impugned claims lack actual utility, in that certain strains of *Aspergillus terreus* have been shown to be unable to produce any of the claimed compounds; and

2. as of the relevant date, the inventors could not soundly predict that the claimed compounds would have the utility promised by the '380 Patent.

[477] Section 2 of the *Patent Act* defines an invention as something that is "new and useful". From this comes the concept of "utility".

[478] A number of principles associated with the law of utility are well established in the jurisprudence. To begin, the overarching concept is that, as of the relevant date, there must have been a demonstration of utility of the invention or, lacking that, a sound prediction of utility based on the information and science available at the time of the prediction (see, for example, *Merck & Co. v. Apotex Inc.*, 2005 FC 755, 41 C.P.R. (4th) 35 at para. 121; *Pfizer Canada Inc. v. Apotex Inc.*, 2007 FC 26, 306 F.T.R. 254 at paras. 36-40, aff'd 2007 FCA 195, 60 C.P.R. (4th) 177, leave to appeal to SCC refused, [2007] S.C.C.A. No. 371 (QL), 381 N.R. 399 (note)).

[479] Apotex bears the burden on this issue of validity. To demonstrate lack of utility, Apotex must show "that the invention will not work, either in the sense that it will not operate at all or, more broadly, that it will not do what the specification promises that it will do" (*Consolboard*, above, at p. 525).

[480] For many patents in the pharmaceutical field, the inventors will not yet have demonstrated that the invention “works”, as of the relevant date. In such cases, the inventors rely on the concept of “sound prediction”. The doctrine of sound prediction can be relied upon by an inventor to justify patent claims whose utility has not actually been demonstrated, but can be soundly predicted based upon the information and expertise available (*Apotex Inc. v. Wellcome Foundation Ltd.*, 2002 SCC 77, [2002] 4 S.C.R. 153 at para. 56 [*Wellcome AZT*]). A party challenging the utility of a patent based on sound prediction must demonstrate that the prediction was not sound or that there is evidence of a lack of utility. As stated in *Wellcome AZT*, above, at paragraph 56:

> If a patent sought to be supported on the basis of sound prediction is subsequently challenged, the challenge will succeed if, *per* Pigeon J. in *Monsanto Co. v. Commissioner of Patents*, [1979] 2 S.C.R. 1108, at p. 1117, the prediction at the date of application was not sound, or, irrespective of the soundness of the prediction, "[t]here is evidence of lack of utility in respect of some of the area covered".

[481] The relevant date is the date of the filing of the Canadian patent application (*Ramipril I (FC)*, above, at paras. 88-96). For the '380 Patent, that date is June 11, 1980.

[482] Where the specification does not promise a specific result, no particular level of utility is required - a "mere scintilla" of utility will suffice (H.G. Fox, *The Canadian Law and Practice Relating to Letters Patent for Inventions* (4th ed., 1969), at p.153). However, as stated in *Consolboard*, above, where the specification sets out an explicit "promise", utility must be measured against that promise (see, for example, *Pfizer Canada Inc. v. Canada (Minister of Health)*, 2008 FCA 108, 67 C.P.R. (4th) 23 at para. 53 [*Pfizer Atorvastatin (FCA)*]). In other words, does the invention do what the patent promises it will do? The question to consider is whether, at the date of filing, the patentee had sufficient information upon which to base the promise. If not, the patentee must have had sufficient information upon which to make a sound prediction of the promise.

[483] At paragraph 70 of *Wellcome AZT*, above, the Supreme Court of Canada articulated a three-part test that must be satisfied in order to establish that a sound prediction has been made by the an inventor. The three elements of the test are:

1. there must be a factual basis for the prediction;

2. the inventor must have an articulable and "sound" line of reasoning from which the desired result can be inferred from the factual basis; and

3. there must be proper disclosure.

[484] To be sound, a prediction does not need to amount to certainty, as it does not exclude the risk that some compounds within the area claimed may, at some later time, prove to be devoid of utility.

[485] With these principles in mind, I turn to the '380 Patent and the evidence before me.

(2) The '380 Patent

[486] As of the relevant date of June 11, 1980 (the Canadian filing date), Merck had made, but not tested, the compounds for which the process is claimed. In other words, it was not relying on actual utility but on its prediction that the four compounds would have utility.

[487] As noted, sound prediction must be measured against the promise of the patent, where one is explicitly expressed or may be implied. The promise of the '380 Patent is discussed in Section V of these Reasons. To review, I have concluded the following:

1. The '380 Patent does not promise that all micro-organisms within the species *Aspergillus terreus* will produce the four compounds of claim 1 or the compounds identified in the other disputed claims.

2. The patent does promise that the compounds produced by the fermentation process identified in the patent are “useful as antihypercholesteremic agents for the treatment of atherosclerosis, hyperlipemia and like diseases in humans”.

[488] I will measure the utility of the '380 Patent against these two promises.

(3) Lack of Utility

[489] Apotex claims that it has presented empirical evidence of inutility of claims 1, 2 and 5. This assertion of inutility is founded on testing, by Drs. Sorenson and Samson, that demonstrated that not all strains of micro-organisms within the genus *Aspergillus* or – more narrowly – within the species *Aspergillus terreus* are capable of producing the claimed compounds.

[490] Dr. Sorensen was asked, by counsel for AFI, to investigate the ability of different strains of *Aspergillus terreus* to produce lovastatin. He was instructed to use fermentation conditions and media contemplated or specifically taught in the '380 Patent. He designed experiments involving four different strains of *Aspergillus terreus*. Two of those strains (referred to as A18 and R99) were strains which had previously been shown to produce Compound I. The other two strains (referred to as UAMH 7844 and UAMH 9313) were obtained by Dr. Sorensen from the University of Alberta Microfungus Collection and Herbarium (UAMH). In simple terms, Dr. Sorensen’s results were as follows:

- lovastatin (Compound1) was detected in the A18, R99 and UAMH 9313 extracts;

- lovastatin was not detected in the UAMH 7844 extract; and

- no quantifiable quantities of dihydrolovastatin (Compound II) were detected in any of the four extracts.

[491] Similar results were obtained by Dr. Samson, who also carried out testing of certain micro-organisms at the request of counsel for AFI. Dr. Samson found that:

- A18, R99 and a strain identified as Merck ATCC 20542 produced lovastatin;

- a strain identified as *Aspergillus terreus* IBT 20944 produced no detectable quantities of lovastatin; and

- a strain identified as *Aspergillus alabamensis* (which, according to Dr. Samson, would have been classified as *Aspergillus terreus* in 1984) produced no detectable quantities of lovastatin.

[492] Witnesses presented by Merck did not dispute the core of these findings. Dr. Alberts, one of the named inventors, acknowledged that not all *Aspergillus terreus* strains tested by Merck produced lovastatin. Dr. Lasure agreed that some strains of *Aspergillus terreus* would not produce lovastatin. In Apotex's view, the result must be that claims 1, 2 and 5, and each of the dependent product claims 13 to 15, are invalid since they include embodiments that will not achieve the promised result.

[493] The problem with this argument is that Apotex relies on a construction and promise of the '380 Patent with which I do not agree. During final argument, Apotex conceded that their assertion is established assuming that “my friend’s construction is not adopted”.

[494] For the reasons expressed in my analysis of proper claims construction, I have concluded that: (a) the claims only include micro-organisms that fall within the species *Aspergillus terreus*; (b) the '380 Patent does not promise that all micro-organisms within the species *Aspergillus terreus* will produce lovastatin; and, (c) none of claims 1, 2 and 5 requires that all four (or two, where applicable) compounds be produced from each fermentation. Thus, it is irrelevant that that Drs. Sorenson and Samson found strains of *Aspergillus terreus* which were incapable of producing lovastatin and that other strains could only produce lovastatin (Compound I).

[495] Apotex has failed to meet its burden to demonstrate that "[t]here is evidence of lack of utility in respect of some of the area covered" (*Wellcome AZT*, above, at para. 56).

(4) Sound Prediction

[496] As noted above, Apotex may satisfy its burden of showing a lack of utility even where it cannot demonstrate inutility. Its burden can be met by demonstrating, on a balance of probabilities, that the prediction of the inventors was not sound. I turn now to a consideration of whether the three elements of the test for sound prediction, as set out in *Wellcome AZT*, above, have been met.

[497] In determining that the requirements for sound prediction had been met, the Court in *Wellcome AZT* found that the factual basis for the sound prediction of a new use compound rested upon the *in vitro* test results of AZT against the HIV in a human cell line along with Glaxo's data on AZT, including animal tests (above, para. 72). The line of reasoning was found to be Glaxo's knowledge of the mechanism for the reproduction of a retrovirus.

(a) *The Factual Basis*

[498] The question of sound prediction is one of fact (*Wellcome AZT*, above, at para. 71). The inventors must be able to show that, at the relevant time, they were in possession of a factual basis upon which they could articulate the desired result. The perspective being examined at this stage is a subjective one. The knowledge, activities and endeavours of the inventors themselves must be considered.

[499] In this case, Merck’s key witness was Mr. Alfred W. Alberts, one of the named inventors of the '380 Patent. In credible testimony, Mr. Alberts told the “story” of the invention that became the '380 Patent.

[500] The '380 Patent story began in 1975, when Mr. Alberts arrived at Merck and began working in the area that was called “basic research”. He established a new department within that domain, a department that was called “biochemical regulation”. The mandate of the department was to take a rational approach to the development of new drugs. Mr. Alberts described the approach as follows:

> The approach that I was brought in to do was to go and do a – go back to the beginning, find the -- to break down the system, find the key targets for the disease, and then start from there with discovering -- hopefully discovering compounds that affect the disease process by working at the very simple, basic level, and then moving up from there to animal studies.

[501] One area of research for the department was cholesterol biosynthesis. According to Mr. Alberts, it was well known, by 1975, that cholesterol was intimately involved with the atherosclerotic process. The pathway of cholesterol biosynthesis was understood in 1975 and was described by Mr. Alberts as follows:

> The pathway of cholesterol biosynthesis is very complex. This is just a brief summary highlighting the salient features of the process.
> It starts with a simple two carbon compound known as acetate and which is basically the salt of vinegar.
>
> It's activated to a compound known as acetyl coenzyme A/acetyl CoA.
>
> Then in a series of steps, three acetyl CoA units are joined together to form the compound known as hydroxymethylglutaryl coenzyme A/HMG-CoA, which is converted by an enzyme known as HMG CoA reductase to mevalonic acid. And I will refer -- sometimes refer to it as mevalonic acid or the salt form, which is mevalonate. And this six carbon compound in a series of condensations ends up as the 30 carbon compound, squalene, which is then modified into the 27 carbon sterol lipid cholesterol.

[502] The Merck scientists were the first to isolate mevalonic acid – described by Mr. Alberts as “the potential missing link in the cholesterol pathway”.

[503] Based on their knowledge of this pathway, the Merck scientists were looking for compounds that could break this chain. One part of the biosynthesis that was of interest was the hydroxy-methylglutaryl-coenzyme A reductase (known as HMG-CoA reductase) stage. The

scientists understood that, if a compound could inhibit or blocked the synthesis of cholesterol at the HMG-CoA reductase stage, there would be no conversion of: (a) HMG CoA reductase to mevalonic acid; (b) mevalonic acid to squalene; and, (c) squalene to cholesterol.

[504] The Merck scientists first became aware of compounds that inhibited HMG-CoA reductase in early 1976, when:

> We received at Merck a correspondence from a representative in Japan who came across a newly issued, newly published patent in Japan describing an inhibitor of HMG-CoA reductase known as ML-236B and also became known as Compactin.

[505] A sample of compactin was received from Sankyo Company in Japan. In addition, Dr. Akira Endo of the Sankyo Company visited Merck on August 26, 1977. According to notes of the meeting, Dr. Endo presented data with respect to ML-236B (compactin). It was stated that the compound "inhibits de novo cholesterol biosynthesis and reduces serum cholesterol when administered orally [in rats]." This compound operated as an HMG-CoA reductase inhibitor.

[506] The goal was clearly to develop a compound that would be as good as or better than compactin. Beginning in January 1978, the Merck scientists introduced a new *in vitro* assay, the HMG-CoA reductase assay. This allowed the measurement of the inhibition of HMG-CoA reductase by any tested micro-organism. ML-236B (compactin) was the benchmark against which the activity of organisms from the Merck chemical library were measured. Between January 1978 and November 1978, none of a large number of tested micro-organisms met the goal.

[507] As reflected in the laboratory notebooks and in Mr. Alberts's testimony, November 7, 1978 was a turning point. In the first week of November 1978, Mr. Alberts's group received samples 18 and 19 (F 4683 and F 4684), both of which demonstrated inhibitory activity in the HMG-CoA reductase assay.

[508] From that point, the most important steps can be summarized as follows.

- On November 27, 1978, Mr. Alberts strongly recommended that Merck further pursue "the isolation and characterization of the inhibitory component in F 4683 for use as a potential hypocholesterolemic agent".

- In December 1978, another sample – F 4797 – was found to have inhibitory activity that was tenfold higher than the first culture, F 4683.

- On February 12, 1979, the structure of lovastatin, the lactone (L-154,803), was recorded by Dr. Albers-Schonberg; the structure was similar to compactin.

- On February 12, 1979, Dr. Otto Hensens identified and recorded the structure of the open dihydroxy acid form of lovastatin.

- On February 13, 1979, Ms. Chen assayed the two samples used to identify the structures above and confirmed that they were inhibitory.

- On February 16, 1979, Mr. Alberts signed the Merck Confidential Memorandum of Invention (referred to below).
- On August 1, 1979, the structure of the natural dihydro (Compound II of the '380 Patent) was identified and recorded by Dr. Otto Hensens, having been found active in the HMG-CoA reductase assay on July 31, 1979.

- On August 2, 1979, a hydrolyzed version of the natural dihydro, being the open hydroxyl acid (Compound IV of the '380 Patent), was assayed and also found to be active in the HMG-CoA reductase assay.

[509] On February 16, 1979, Dr. Alberts completed a “Confidential Memorandum of Invention”, on behalf of the inventors. This Memorandum summarizes the work of the inventors. The structure of Compound I, a “homolog” of ML-236B (compactin), “produced by an *Aspergillus*” is described. The inventors explicitly note the utility or proposed use of the invention as “hypocholesteremic, antifungal”. As of the date of the Memorandum, the inventors had found that the compound had “*in vitro* potency similar to ML-236B as inhibiting HMG-CoA reductase.”

[510] Apotex’s main criticism of Merck’s work relates to what was not done by the Merck scientists. Apotex submits that, because there was no testing of the compounds on humans before the Canadian filing date, Merck was missing a critical piece of factual information. In Apotex’s view, without this information, the inventors did not have an adequate factual basis for the prediction that the compounds would be “useful as antihypercholesteremic agents for the

treatment of atherosclerosis, hyperlipemia and like diseases in humans." However, when cross-examined on this issue, Mr. Alberts was clear as to how Merck reached its prediction, even though human trials had not taken place by the Canadian filing date.

> Q. Based on the test results that you had obtained, the in vivo animal test results you'd obtained, would you not agree that you could not reliably predict that Lovastatin was going to be an effective treatment for hypercholesteremia in humans?
>
> A. The only way I could answer that is with any drug before it's been tested in humans, whether it's Lovastatin, whether it's an antibiotic, no matter what it is, you can not reliably predict it's going to work in humans until you put it into the humans, and that is irrespective of the drug.
>
> Q. In terms of these particular models, these animal results, is it not fair to say that these animal models, as a predictor of activity in humans, could not be relied upon to make a sound an assessment of its potential effectiveness?
>
> A. There was enough -- let me go to one animal model that was a good predictor there, and that's the dog, because the dog responds very nicely to the other cholesterol lowering drug, cholestyramine; in fact, it's one of the few models that responds to cholestyramine. Humans respond to cholestyramine. Rats do not respond to cholestyramine. Dogs do. Humans do. So there was a reasonable assumption that a drug that did not lower cholesterol in the rats would conceivably work in humans and based on the biology, based on the biochemistry of the system, it was a reasonable prediction that it would work and based on our knowledge of Compactin. So we had a whole body of evidence that suggested it would work.

[511] I agree with Mr. Alberts; the inventors had a whole body of evidence that suggested that the compounds would work in humans. The inventors had an adequate factual basis for their predictions.

(b) *Line of Reasoning*

[512] I next consider whether Apotex has shown that there was no articulable line of reasoning from which the desired results could be inferred from the factual basis. The question is: given the experimentation and laboratory results that formed the factual basis together with information drawn from the prior art, could Merck reasonably infer that the compounds would meet the promise of being "useful as antihypercholesteremic agents for the treatment of atherosclerosis, hyperlipemia and like diseases in humans"?

[513] There was little expert evidence produced by either side that speaks directly to the question of sound prediction or the line of reasoning. Some assistance was provided by Dr. Gotto, who described his own observations and the findings of scientists in the mid to late 1970s which demonstrated the link between high cholesterol and atherosclerosis.

[514] It was also known at the relevant time that HMG-CoA was the enzyme in the liver responsible for making cholesterol.

[515] Obviously, an essential element in the chain is an understanding of cholesterol biosynthesis. No expert presented an alternative to Mr. Alberts's description of the biosynthesis pathway. It follows, from an understanding of cholesterol biosynthesis, that a compound that can prevent the completion of this pathway – at any stage – will have a good chance of preventing the formation of cholesterol. Thus, it would have been part of the line of reasoning for the

development of all statins, such as lovastatin, that a compound that could inhibit HMG-CoA *in vivo* could be predicted to lower cholesterol in humans.

[516] The next step in the chain of reasoning is the key element – that is, compactin. The Merck inventors knew about the behaviour of compactin. Compactin works on the cholesterol biosynthesis at the HMG CoA reductase stage; it inhibits or prevents the enzyme from producing mevalonic acid. From the disclosure contained in the Endo Patent, the Merck scientists had knowledge of the *in vivo* activity of compactin.

[517] The inventors also knew that the structure of the compounds that they had developed from fermentation of *Aspergillus terreus* was similar to the structure of compactin. It was not unreasonable for the inventors to predict that a compound with a similar structure to compactin would have similar inhibitory properties. Strengthening this prediction, the Merck scientists also had their own *in vitro* testing data that demonstrated activity. All of this information was available to the inventors of the '380 Patent as of February 12, 1979. This reasoning was confirmed by Dr. Gotto during cross-examination:

> Q. Let me ask you this. If in 1979 a compound had been found that could inhibit HMG-CoA reductase in a cell culture in vitro, would one be able to know whether or not that compound would be effective in treating atherosclerosis, hyperlipidemia or those kinds of diseases in humans?
>
> A. Based on the knowledge that one had about Compactin, yes.

[518] In my view, an articulable line of reasoning has been demonstrated. In other words, by February 12, 1979, the inventors of the '380 Patent could soundly predict that the compounds of

the invention would provide treatment for hypercholesteremia in humans based on the known *in vivo* activity of the closely-related compound, compactin, and Merck's own *in vitro* data. In other words, there was an articulable line of reasoning from which the desired result – lowering of cholesterol in humans – could be inferred from the factual basis. This was over a year in advance of the Canadian filing date of June 11, 1980.

[519] Moving forward from February 1979, the Merck scientists were able to add even more information to support the articulable line of reasoning. By July 1979, Merck had supplementary *in vivo* data that confirmed cholesterol synthesis inhibition in rats. Well in advance of the Canadian filing date, Merck had obtained positive results in dogs. This information, while not essential to the sound prediction as of the Canadian filing date, certainly provides additional support for the prediction.

(c) *Disclosure*

[520] The final element of sound prediction is "disclosure". The question is: in the '380 Patent, has Merck provided disclosure of the factual basis and the line of reasoning? I believe that it has.

[521] In *Eli Lilly Canada Inc. v. Apotex Inc.*, 2009 FCA 97, 78 C.P.R. (4th) 388 at para. 18, leave to appeal to SCC refused, [2009] S.C.C.A. No. 219 (QL), 401 N.R. 400 (note)) [*Eli Lilly Raloxifene (FCA)*], the Court of Appeal (referring to *Wellcome AZT*, above) stated that, "where the claimed invention had not yet actually been reduced to practice, the patent must provide a

disclosure such that a person skilled in the art, given that disclosure, could have as the inventors did, soundly predicted that the invention would work once reduced to practice."

[522] Apotex's argument of inadequate disclosure involves two discrete areas: the first is the adequacy of disclosure of factual underpinnings of the invention, and the second is the adequacy of disclosure of methods for producing the claimed compounds from strains of *Aspergillus*.

[523] With respect to the first argument, Apotex asserts that many of the facts that were stated by Dr. Alberts to form the basis of the inventors' prediction of utility were not disclosed in the patent. Specifically, Apotex submits as follows:

> However, the only data disclosed in the '380 Patent that could form a "factual basis" for the predicted utility of the compounds as anti-hypercholesteremic agents are the tests reported in the examples. None of these tests evaluated the capacity of a test compound to lower serum cholesterol levels in mammals or humans. None of the compounds is shown to have been tested in an animal model to determine whether it lowered serum cholesterol. There is no reference or explanation of the rate-limiting role of the HMG-CoA reductase enzyme. There is no disclosure of the knowledge that Merck acquired from its work with compactin, and no disclosure of any relationship between the compounds of the invention and cholestyramine, or why (and how) the properties of cholestyramine would inform a prediction of utility. There is also no data about the toxicology, pharmacokinetics or bioavailability of the compounds that would enable the skilled addressee to predict that the compounds could be effectively administered and tolerated by humans over the identified range of dosage strengths. Accordingly, virtually all of the "facts" Dr. Alberts stated formed the basis of the inventors' prediction of utility are not disclosed.

[524] The first problem with Apotex's argument is that it is based on a requirement that the patent disclose data to support the promise. The question of whether or not a patentee has

obtained enough data to substantiate its invention is an irrelevant consideration with respect to the application of subsection 27(3) of the *Act*. The Court is concerned with the sufficiency of the disclosure, not the sufficiency of the data underlying the invention (*Pfizer Atorvastatin* (*FCA*), above, at para. 56).

[525] Apotex also refers to the animal testing carried out by Merck in 1979. Reference is made to the testimony of Mr. Alberts where he agreed that the testing of dogs led Merck to believe that lovastatin would result in cholesterol reduction in humans. The '380 Patent does not disclose this testing. Thus, Apotex submits that the failure to disclose the existence and results of such tests establishes that there is insufficient information disclosed in the '380 Patent to justify the prediction. I do not agree with either Apotex's characterization of Mr. Alberts's testimony or the inference that they draw.

[526] Apotex relies on *Eli Lilly Raloxifene (FC)*, above. In that case, Justice Roger Hughes, the trial judge, found, as a matter of fact, that Merck had placed reliance on a paper published before the Canadian filing date (the Hong Kong study). Justice Hughes concluded that the requirement for disclosure had not been met; the Court of Appeal agreed in *Eli Lilly Raloxifene FCA*, above, at paragraph 17. As noted by the Court of Appeal in *Eli Lilly Raloxifene FCA*, at paragraph 15, "As the prediction was made sound by the Hong Kong study, this study had to be disclosed." In my view, the situation before me is distinguishable.

[527] I agree that the cross-examination of Mr. Alberts resulted in a list of facts and information that the inventors of the '380 Patent knew as of the Canadian filing date. One of the

areas of interest relates to the dog studies carried out in 1979. Apotex pounces on this information as something that ought to have been disclosed in the '380 Patent in order to justify the sound prediction. However, I do not understand the jurisprudence to teach that the patent specification must disclose absolutely everything that that the inventor knew up to the relevant date. In *Eli Lilly Raloxifene (FC)*, above, without disclosure of the Hong Kong study, a skilled person would not have had sufficient information to understand the justification for the prediction. We must examine the specification to determine whether, with the information disclosed (even if there was more information available and undisclosed), a skilled person could have soundly predicted that the invention would work once reduced to practice.

[528] In the case of the '380 Patent, the question is whether sufficient information was disclosed to allow the skilled person to soundly predict that the compounds of the invention would be “useful as antihypercholesteremic agents for the treatment of atherosclerosis, hyperlipemia and like diseases in humans”.

[529] What was disclosed in the '380 Patent? The '380 Patent contains the following disclosures:

- the association between atherosclerosis and high cholesterol (p. 2, lines 11-15);

- the utility of inhibiting cholesterol biosynthesis (p. 2, lines 14-16);

- prior art consisting of US patents for compactin, a fermentation product obtained from the genus *Penicillium*, which compound was found to be an inhibitor, *in vivo*, of the biosynthesis of cholesterol (p. 2, lines 17-26);

- the discovery by the inventors of the '380 Patent that compounds produced from *Aspergillus* are more potent inhibitors of cholesterol synthesis *in vivo* than compactin (p. 2, lines 28-33; p. 3, lines 1-5);

- the fact that HMG-CoA reductase inhibition is the relevant means of inhibiting cholesterol biosynthesis (p. 14, lines 30-35);

- the structure of lovastatin and the other compounds (p. 9, 10, 11 and 12);

- *in vitro* HMG-CoA reductase inhibition by lovastatin, (p. 14, line 30; p. 15, line 6; p. 24, lines 7-8; p. 25, lines 10-12; p. 42, lines 1-13); and

- *in vivo* inhibition of cholesterol synthesis by Compound II (p. 42, lines 15-25).

[530] Taken as a whole, I am not persuaded that there was inadequate disclosure. A skilled person would conclude that the '380 Patent sufficiently discloses the factual basis and the line of reasoning to soundly predict that the claimed compounds would be useful in the treatment of high cholesterol. In other words, as required by the jurisprudence, the '380 Patent discloses the factual basis and line of reasoning for its promise. The prediction was made sound by the

information disclosed; the disclosure of other information within the knowledge of the inventors was not essential to the prediction.

[531] The second of Apotex's submissions is that the '380 Patent fails to disclose the methods for determining which strains of the genus *Aspergillus* will produce the desired compounds. As discussed in the section of these reasons on claims construction, I have concluded that the patent only claims compounds produced from *Aspergillus terreus* and, further, that it does not promise that lovastatin can be produced from all strains of *Aspergillus terreus*. Apotex argues that, even on this narrower construction and promise, Merck was required to disclose the methods for identifying producing strains. Apotex argues that the specification does not disclose this information and that to find the producing strains would require excessive and inventive experimentation by the skilled person.

[532] The courts have recognized that "routine trials and experiments not amounting to new inventions might be required to put [an invention] into practice" (*Proctor & Gamble Co. v. Bristol-Myers Ltd.*(1978), 39 C.P.R. (2d) 145 at para. 51, [1978] F.C.J. No. 812 (QL) (F.C.T.D.); see also, *Mobil Oil Corp. v. Hercules Canada Inc.* (1995), 63 C.P.R. (3d) 473, [1995] F.C.J. No. 1243 (QL) (F.C.A.)); *Aventis Pharma Inc. v. Apotex Inc*. 2005 FC 1283, 43 C.P.R. (4th) 161 at para. 207). The evidence before me does not support Apotex's assertion that inventive experimentation would be required to find producing strains of *Aspergillus terreus*. I have already discussed this issue (see paragraphs 57 to 130) under claims construction. To repeat, I am satisfied that the skilled person could use well-known techniques to rapidly screen a large number of isolates of strains of *Aspergillus terreus* to determine which strains are producing.

Moreover, since, on my construction, the claims are limited to strains of the species *Aspergillus terreus*, there are manageable boundaries on the testing that would be required.

D. *First Inventorship/Missed Conflict*

(1) Introduction

[533] Apotex submits that the Merck inventors were not the first inventors of the compound lovastatin as claimed in the '380 Patent and that, therefore, the '380 Patent should be invalidated on the basis that the “invention” of the '380 Patent was known or used as of the date of filing the patent application. In so arguing, Apotex recognizes that it must overcome the requirements of the *Patent Act*.

[534] The patent application that resulted in the issuance of the '380 Patent was patent application No. 353, 777 filed with the Patent Office on June 11, 1980 (the Monaghan Application). Apotex submits that the Monaghan Application disclosed the invention of lovastatin and ought to have been placed into conflict with patent application No. 345, 983 (the Endo Application), which was filed with the Patent Office on February 19, 1980. The Endo Application ultimately resulted in the issuance of the ‘794 Patent.

(2) Legal Principles

[535] Prior to 1989, the overall scheme under the *Patent Act* was one of first to invent. By contrast, the scheme under the *Patent Act* currently in force can be described as first to file. The notion of first inventorship is embodied in s. 27(1) of the *Act*:

27. (1) Subject to this section, any inventor or legal representative of an inventor of an invention that was (a) not known or used by any other person before he invented it, (b) not described in any patent or in any publication printed in Canada or in any other country more than two years before presentation of the petition hereunder mentioned, and (c) not in public use or on sale in Canada for more than two years prior to his application in Canada, may, on presentation to the Commissioner of a petition setting out the facts, in this Act termed the filing of the application, and on compliance with all other requirements of this Act, obtain a patent granting to him an exclusive property in the invention.	Sous réserve des autres dispositions du présent article, l'auteur de toute invention ou le représentant légal de l'auteur d'une invention peut, sur présentation au commissaire d'une pétition exposant les faits, appelée dans la présente loi "le dépôt de la demande", et en se conformant à toutes les autres prescriptions de la présente loi, obtenir un brevet qui lui accorde l'exclusive propriété d'une invention qui n'était pas : a) connue ou utilisée par une autre personne avant que lui-même l'ait faite; b) décrite dans un brevet ou dans une publication imprimée au Canada ou dans tout autre pays plus de deux ans avant la présentation de la pétition ci-après mentionnée; c) en usage public ou en vente au Canada plus de deux ans avant le dépôt de sa demande au Canada.

[536] Recognizing that more than one person might claim inventorship to similar or overlapping subject matters, Parliament provided means for identifying and resolving such a conflict. To begin, s. 43(1) of the *Act* defines when a conflict exists:

Conflict between two or more pending applications exists (a) when each of them contains one or more claims defining substantially the same invention; or (b) when one or more claims of one application describe the invention disclosed in one of the other applications	Se produit un conflit entre deux ou plusieurs demandes pendantes dans les cas suivants: a) chacune d'elles contient une ou plusieurs revendications qui définissent substantiellement la même invention; b) une ou plusieurs revendications d'une même demande décrivent l'invention divulguée dans l'autre ou les autres demandes

The balance of s. 43 sets out the procedures for declaring and dealing with a conflict.

[537] While s. 27(1) gives the right to a patent to the first inventor, the *Act* also contemplates that legal proceedings may be brought with respect to the validity of patents (see the *Patent Act*, starting at s. 53). In particular, s. 59 of the *Act* permits a defendant (such as Apotex) in a patent infringement action to plead "any fact or default which by this *Act* or by law renders the patent void." Under s. 60(1) of the *Act*, a patent or any claim in a patent may be "declared invalid or void by the Federal Court ... at the instance of any interested person."

[538] However, when the validity of a patent is being challenged on the question of inventorship, s. 61(1) is a limiting or qualifying provision. In the case before me, s. 61(1)(b) is relevant:

No patent or claim in a patent shall be declared invalid or void on the ground that, before the invention therein defined was made by the inventor by whom the patent was applied for, it had already been known or used by some other person, unless it is established that	Aucun brevet ou aucune revendication dans un brevet ne peut être déclaré invalide ou nul pour la raison que l'invention qui y est décrite était déjà connue ou exploitée par une autre personne avant d'être faite par l'inventeur qui en a demandé le brevet, à moins qu'il ne soit établi que, selon le cas :
(b) that other person had, before the issue of the patent, made an application for patent in Canada on which conflict proceedings should have been directed;	b) cette autre personne avait, avant la délivrance du brevet, fait une demande pour obtenir au Canada un brevet qui aurait dû donner lieu à des procédures en cas de conflit;

[539] As stated in s. 61(1)(b), no patent will be declared invalid on the grounds of prior inventorship by some other person unless the challenging party can establish that the other person had, before the issue of the patentee's patent, made an application for a patent in Canada on which conflict proceedings should have been directed. Stated in other words, a party may only successfully raise inventorship as an issue if: (a) the invention in the patent or claim had already "been known or used by some other person"; (b) the other person made a patent application for this prior invention in Canada; or (c) "conflict proceedings should have been directed". The interpretation of s. 61(1)(b) was the subject of discussion in the case of *Laboratoires Servier v. Apotex Inc.*, 2008 FC 825, 67 C.P.R. (4th) 241 [*Servier FC*] .

[540] Thus, the threshold question to be answered is whether, on the facts before me, there was a “missed conflict”. In other words, should conflict proceedings have been directed between the Endo Application and the Monaghan Application? If there was no missed conflict, Apotex is precluded, by s. 61(1)(b), from challenging the validity of the '380 Patent on the grounds of prior inventorship.

(3) Was there a missed conflict

[541] The Endo Application was filed on February 19, 1980; the Endo Patent was issued on August 17, 1982. The Monaghan Application was filed on June 11, 1980; the ‘380 Patent was issued on January 31, 1984. Conflict could have been declared only during the co-pendency of the two applications; that is, between June 11, 1980 and August 17, 1982.

[542] A review of the case or file history for the '380 Patent provides us with the sequence of events leading to the issuance of the patent.

[543] As filed, claims 1 to 7 of the Monaghan Application were claims to processes for producing certain compounds. However, claim 8 was for Compounds I and II alone and claim 9 was for Compounds III and IV alone. Claims 10 to 19 were claims to salts, esters and compounds all of which were dependent on claims 8 or 9. While claims 1 to 7, as filed, were product-by-process claims, claims 8 to 19 did not contain process restrictions; they were what is referred to as *per se* claims. The problem with *per se* claims is that they were not permissible under the *Patent Act*, as it

existed at the relevant time. Specifically, s. 41(1) (later, s. 39(1)) of the *Patent Act*, as it stood in 1982) stated that:

In the case of inventions relating to naturally occurring substances prepared or produced by, or significantly derived from, microbiological processes and intended for food or medicine, the specification shall not include claims for the resulting food or medicine itself, except when prepared or produced by or significantly derived form the methods or processes of manufacture particularly described and claimed. [Emphasis added.]	Lorsqu'il s'agit d'inventions couvrant des substances que l'on trouve dans la nature, préparées ou produites, totalement ou pour une part notable, selon des procédés microbiologiques et destinées à l'alimentation ou à la médication, aucune revendication pour l'aliment ou le médicament ne doit être faite dans le mémoire descriptif, sauf pour celui ainsi préparé ou produit selon les modes du procédé de fabrication décrits en détail et revendiqués. [Non souligné dans l'original.]

In simple terms, the inventors of the Monaghan Application could never have received a patent that included claims 8 to 19, as originally filed.

[544] In a letter from the Patent Office dated November 10, 1982 (Office Action), counsel for the Monaghan Application was advised of the problem:

> The claims of this application are governed by Section 41(1) of the Patent Act. In the case of a substance intended for food or medicine and prepared by a chemical process, an application must have a patentable process claim, and any product claim must be in process-dependent form and of the same scope as the process claim. Amendment or cancellation of claims 8-19 is required.

[545] The response to the Office Action was received by the Patent Office on February 9, 1983. Amended claims 1 through 20 were substituted for the non-allowable claims 8 to 19. Evidently,

the Commissioner of Patents agreed with the submission that the Monaghan Application now contained “claims conforming with the requirements of section 41(1)”; the '380 Patent was issued on January 31, 1984.

[546] Each of Apotex and Merck put forward an expert to speak to the practices of the Patent Office at the relevant times. Both Mr. Robert Barrigar (put forward by Merck) and Mr. Robert Hirons (put forward by Apotex) have been registered patent agents in Canada for a long time. Both have extensive knowledge of Canadian patent prosecution and practice between 1980 and 1982, and are knowledgeable about practices of the Commissioner of Patents at that time. I accepted the qualifications of each to speak to these matters.

[547] Both experts agreed that a declaration of conflict would not have been made between two pending applications when each application contained process-dependent claims for the same compound made using different processes. Accordingly, the question of missed conflict could only have arisen between claims 8 to 19, as originally filed, of the Monaghan Application and some or all of the claims of the Endo Application.

[548] Mr. Hirons opined that the requirements of s. 43(1)(b) of the *Patent Act* were satisfied and a conflict, as defined in that provision, existed between the two applications (Hirons Expert Report, Exhibit 117, para. 13). Mr. Hirons pointed out that, during the period of co-pendency, the compound claims in the Monaghan Application were not restricted by process. Thus, in his view, a conflict between the two applications necessarily existed. In other words, one or more of

claims 8 to 19 of the Monaghan Application described the invention disclosed in the Endo Application and, as a result, the Commissioner should have commenced conflict proceedings.

[549] Frankly, this is, to a large degree, a legal opinion and not one for which I need the assistance of an expert. That being said, I do not disagree with Mr. Hirons's conclusion that a conflict, as defined in s. 43(1)(b), existed as between the two applications. Moreover, Mr. Hirons's description of how conflict proceedings were conducted, once directed, is not inaccurate.

[550] However, Mr. Hirons fails to answer the question of whether "conflict proceedings should have been directed". He assumes that the existence of a conflict automatically requires the Commissioner to direct conflict proceedings. The mere existence of a conflict at the application stage does not, in my view, automatically mean that conflict proceedings should have been directed.

[551] In responding to this question, I refer first to the procedures described in s. 43, in respect of the legal requirements of the *Patent Act*. Sections 43(2) to 43(4) deal with procedures to be followed before a conflict is declared. I accept that, when a s. 43(1) conflict exists, s. 43(2) sets out a mandatory procedure to be followed.

Procedure to be followed before conflict is declared	Procédure à suivre avant déclaration de conflit
(2) When the Commissioner has before him two or more applications referred to in subsection (1), he shall	(2) Lorsque le commissaire a devant lui deux ou plusieurs de ces demandes, il doit :

(a) notify each of the application of the apparent conflict and transmit to each of them a copy of the conflicting claims, together with a copy of this section; and	a) notifier à chacun des demandeurs le conflit apparent, et transmettre à chacun d'' eux une copie des revendications concurrentes, ainsi qu'une copie du présent article;
(b) give to each applicant the opportunity of inserting the same or similar claims in his application within a specified time.	b) procurer à chaque demandeur l'occasion d'insérer dans sa demande les mêmes revendications ou des revendications similaires, dans un délai spécifié.

[552] In this case, assuming that claims 9 to 19 of the Monaghan Application, as originally filed, were in conflict with some or all of the claims in the Endo Application, the Commissioner was required to follow the procedure set out in s. 43(2) of the *Act*. He did not do so in this case. However, these are steps to be taken before the declaration of conflict to determine if there should be a formal declaration. Thus, even if the Commissioner erred by not complying with the mandatory provision, any such error would be of no moment if, at the end of the day, there was no need to make a formal declaration of conflict. The next step – the formal declaration – is set out in s. 43(5):

Formal declaration of conflict	Déclaration formelle de conflit
(5) Where the subject matter of the claims described in subsection (3) is found to be patentable and the conflicting claims are retained in the applications, the Commissioner shall require each applicant to file in the Patent Office, in a sealed envelope duly endorsed,	(5) Si l'objet des revendications visées au paragraphe (3) est reconnu brevetable et que les revendications concurrentes sont maintenues dans les demandes, le commissaire exige de chaque demandeur le dépôt, au Bureau des brevets, dans une

within a time specified by him, an affidavit of the record of invention, which affidavit shall declare	enveloppe scellée portant une suscription régulière, dans un délai qu'il spécifie, d'un affidavit du relevé de l’invention. L'affidavit déclare :
(a) the date at which the idea of the invention described in the conflicting claims was conceived;	a) la date d laquelle a été conçue l’idée de l'invention décrite dans les revendications concurrentes;
(b) the date on which the first drawing of the invention was made;	b) la date laquelle a été fait le premier dessin de l’invention;
(c) the date when and the mode in which the first written or oral disclosure of the invention was made; and	c) la date i laquelle a été faite 1a première divulgation écrite ou orale de !'invention et la manière dont elle a été faite;
(d) the dates and nature of the successive steps subsequently taken by the inventor to develop and perfect the invitation from time to time up to the date of the filing of the application for patent.	d) les dates et la nature des expériences successives que l’inventeur a pratiquées par la suite afro de développer et mettre graduellement an point cette invention jusqu'à la date du dépôt de la demande de brevet,

[553] Of critical importance, this provision establishes that the conflict proceedings described in s. 43(5) and the balance of s. 43 only apply “where the subject-matter of the claims described in subsection (3) is found to be patentable and the conflicting claims are retained in the applications.”

[554] Relating the file history to the co-pendency period between the Endo Application and the Monaghan Application, at no time between June 11, 1980 and August 17, 1982 was the Monaghan Application in a patentable form. Quite simply the potentially-conflicting *per se*

claims of the Monaghan Application were not patentable; claims 8 to 19 did not contain claims that met the requirements of the *Patent Act*. The subject matter of claims 8 to 19 was not patentable. In short, during the co-pendency period, there was no obligation on the Commissioner to declare a conflict.

[555] My understanding of s. 43 of the *Patent Act* is consistent with the practices of the Patent Office. Mr. Barrigar, using his experience and knowledge of processes in the Patent Office, provided his opinion on how, in practical terms, the Patent Office would have dealt with the two patent applications. This portion of his Expert Report and his oral testimony were very helpful. In brief, the Patent Office would not, faced with unpatentable claims, have initiated conflict proceedings. Rather, the practice of the Patent Office was as described by Mr. Barrigar (Barrigar Expert Report, Exhibit 44, para. 18):

> Based on my experience, and consistent with the provisions of the "Old Act", it was the uniform practice of the Patent Office in the period 1980 to and including 1984 to implement conflict practice in the context of the Patent Act as a whole. As discussed more fully below, this meant that only claims satisfying the other requirements of the Act and applicable Patent Rules were placed in conflict. It was the practice of the Patent Office to endeavour to dispose of all other claiming issues before declaring any conflict, so that if possible it would not be necessary to conduct conflict proceedings. Conflict proceedings constituted a drain on Patent Office resources and delayed issue of patents.

[556] Thus, while the Commissioner may “technically” have been required to comply with ss. 43(2) to 43(4) of the *Act*, his failure to do so is without consequence where, as in this case, the requirements to pursue the conflict in formal proceedings, as set out in s. 43(5), were not met. Even Mr. Hirons finally agreed, on cross-examination that:

> There are very good policy reasons why the Commissioner of Patent would not want to launch or commence conflict proceedings in respect of claims that everybody knows cannot be issued in the form they are written.

[557] Apotex asserts that the practice of resolving apparent conflicts, by requiring the applicant to amend all or part of the specification to remove objectionable claims, should have no bearing on the right to invoke s. 61 of the *Patent Act*. I disagree. Where a patent application contains claims that can never result in a patent, there is no conflict to declare.

[558] In summary on this issue, I am satisfied that, on the facts of this case, there was no requirement to direct conflict proceedings between the Endo Application and the Monaghan Application. There was no missed conflict and Apotex is precluded, by s. 61(1)(b) of the *Act*, from challenging the validity of the '380 Patent on the grounds of prior inventorship.

(4) Did the Endo application disclose the invention of the '380 Patent?

[559] If I am incorrect in my conclusion that Apotex is precluded from challenging the validity on the grounds of prior inventorship, I turn to the question of whether the Endo Application and Patent disclose the same invention as that of the '380 Patent.

[560] The Endo Application and Patent clearly refer to a substance called “Monacolin K”. As set out in claim 1, the Endo Patent claims:

> A process for preparing Monacolin K, which process comprises cultivating a Monacolin K-producing micro-organism of the genus *Monascus* in a culture medium therefore.

[561] It is accepted that Monacolin K is lovastatin. However, as discussed earlier in these Reasons, an essential feature of the claims of the '380 Patent is that the lovastatin be made using a strain of the species *Aspergillus terreus*. The invention is lovastatin when made by fermentation of *Aspergillus terreus* and does not include lovastatin made with other micro-organisms. *Monascus* is a different genus from *Aspergillus*. Accordingly, the two applications that included allowable claims did not contain one or more claims defining substantially the same invention. Moreover, neither application described the invention disclosed in the other application.

[562] Thus, even if I accept that there was a missed conflict, the invention of the '380 Patent is not the same as that of the Endo Application or Patent. Apotex has not persuaded me that the invention of the '380 Patent was known or used by Dr. Endo prior to the filing date of the Monaghan Application.

(5) Red Yeast Rice/Anticipation

[563] Apotex submits that claims 13 to 15 of the '380 Patent are invalid pursuant to the principles of “anticipation by prior use”. Briefly stated, Apotex’s argument is that the compound lovastatin (also known as Monacolin K) was known and used in the form of traditional Red Yeast Rice long before the priority date of the '380 Patent or any earlier date of invention. Thus, Apotex alleges that the presence of lovastatin in any Red Yeast Rice product before the priority date of the '380 Patent was anticipatory of claims 13 to 15. In this section, I will use the term

"Red Yeast Rice" to refer to the products, including rice, that are made with the substance known as red yeast.

(a) *Principles of Anticipation*

[564] The concept of anticipation arises from s. 27(1) of the *Patent Act*. Subsection 27(1) permits any inventor to file an application for an invention that was "not known or used by any other person before he invented it". This requirement is echoed in s. 61(1)(a), which allows the Court to invalidate any patent or claim(s) if another person had "disclosed or used the invention in such a manner that it had become available to the public". In short, the *Patent Act* requires that the subject matter of a claim must not have been disclosed to the public before the claim date.

[565] The guiding jurisprudence on the legal test of anticipation is found in the Supreme Court of Canada decision in *Apotex v. Sanofi-Synthelabo*, 2008 SCC 61, [2008] 3 S.C.R. 265 [*Sanofi-Synthelabo*]. At paragraphs 23-27, the Supreme Court teaches that the issue of whether an invention is anticipated by the prior art requires that the Court have regard to two questions:

1. Was the subject matter of the invention disclosed to the public by a single disclosure?

2. If there has been such a clear disclosure, is the working of the invention enabled by that disclosure?

[566] At the first step of the analysis, the Supreme Court provided the following guidance (*Sanofi-Synthelabo*, above, at para. 25):

> When considering the role of the person skilled in the art in respect of disclosure, the skilled person is "taken to be trying to understand what the author of the description [in the prior patent] meant" (para.32). At this stage, there is no room for trial and error or experimentation by the skilled person. He is simply reading the prior patent for the purposes of understanding it.

[567] Once disclosure has been made, the question of enablement was described by the Supreme Court (*Sanofi-Synthelabo*, above, at para 27):

> Once the subject matter of the invention is disclosed by the prior patent, the person skilled in the art is assumed to be willing to make trial and error experiments to get it to work. While trial and error experimentation is permitted at the enablement stage, it is not at the disclosure stage. For purposes of enablement, the question is no longer what the skilled person would think the disclosure of the prior patent meant, but whether he or she would be able to work the invention.

[568] In *Abbott Laboratories v. Canada (Minister of Health)*, 2008 FC 1359, 337 F.T.R. 17 [*Abbott Clarithromycin (FC)*], aff'd 2009 FCA 94, 387 N.R. 347, Justice Hughes undertook a helpful survey of the law of anticipation as it exists after *Sanofi-Synthelabo*, above. He summarized the legal requirements for anticipation as follows (*Abbott Clarithromycin (FC)*, above, at para. 75):

> For there to be anticipation there must be both disclosure and enablement of the claimed invention.
>
> 1. The disclosure does not have to be an "exact description" of the claimed invention. The disclosure must be sufficient so that when read by a person skilled in the art willing to understand what is being said, it can be understood without trial and error.

2. If there is sufficient disclosure, what is disclosed must enable a person skilled in the art to carry out what is disclosed. A certain amount of trial and error experimentation of a kind normally expected may be carried out.

3. The disclosure when carried out may be done without a person necessarily recognizing what is present or what is happening.

4. If the claimed invention is directed to a use different from that previously disclosed and enabled then such claimed use is not anticipated. However if the claimed use is the same as the previously disclosed and enabled use, then there is anticipation.

5. The Court is required to make its determinations as to disclosure and enablement on the usual civil burden of balance and probabilities, and not to any more exacting standard such as quasi-criminal.

6. If a person carrying out the prior disclosure would infringe the claim then the claim is anticipated.

[569] The date for assessment of anticipation is June 15, 1979, the priority date of the '380 Patent.

(b) *Background on Red Yeast Rice*

[570] It is undisputed that Red Yeast Rice (or similar products containing red yeast, such as red yeast bean curd) has been used produced and consumed in Asian countries for hundreds of years. Dr. Scott Harding, an expert witness presented by Apotex, described the uses of Red Yeast Rice in (mainly) Chinese culture as follows (Harding Expert Report, Exhibit 115, para. 15):

> [Red Yeast Rice] has traditionally been used as a specialty food, as a dye or food pigment and as a natural remedy for gastrointestinal infections and diseases of the blood.

[571] According to Dr. Harding, more recently, Red Yeast Rice has been marketed as a product that can lower lipid levels and reduce cardiovascular risk.

(c) *Legal Consequences of lovastatin in Red Yeast Rice*

[572] The expert testimony of Dr. Harding is to the effect that Red Yeast Rice is not and was not produced from *Aspergillus terreus*. Dr. Harding opined that traditional Red Yeast Rice was produced through fermentation of certain strains of species from the genus *Monascus*.

[573] Since Red Yeast Rice does not involve the use of *Aspergillus terreus* in any way, it cannot have been an anticipatory disclosure of the process claims of the '380 Patent. As discussed in the section of these reasons on claims construction, claims 1 to 12 are process claims in which producing strains of *Aspergillus terreus* are fermented to produce certain compounds (including lovastatin as Compound I). Apotex does not assert the argument of anticipation against claims 1 to 12; rather it limits it argument to the product-by-process claims 13 to 15.

[574] Claim 13 is a claim to any one of Compounds I to IV, when prepared by the process defined in claim 1 or by an obvious chemical equivalent. Claim 14 is a claim to one of Compound I or II, when prepared by the process defined in claim 2 or by an obvious chemical equivalent and claim 15 is a claim to one of Compound III or IV, when prepared by the process defined in claim 5, or by an obvious chemical equivalent. Earlier in these reasons, I construed claims 13 to 15 to require that, as an essential element, the product (be it Compound I, II, III or

IV) is produced by the process defined in the earlier claims. Specifically, the compounds of claims 13 to 15 must be made from the fermentation of a species of *Aspergillus terreus*.

[575] For the moment, I will assume that lovastatin could be found in Red Yeast Rice as of the priority date. I accept the opinion of Dr. Harding that Red Yeast Rice is a result of the fermentation of species within the genus *Monascus*. If the allegedly anticipatory product – lovastatin found in Red Yeast Rice – is produced from something other than *Aspergillus terreus,* it cannot, in my view, meet the legal test for anticipation. Stated in terms of the test, Red Yeast Rice does not meet the first requirement that the prior invention must disclose the subject matter of claims 13 to 15.

[576] Apotex responds to this analysis by asserting that a product-by-process claim is a claim to the product. In the words of Apotex:

> Where the product was previously known and a new process for making it has been discovered, the only invention that can be claimed is the process because the product is not "new". Thus, a product-by-process claim can be anticipated by prior disclosure of the product but not of the process.

Apotex relies on the Supreme Court decision in *Hoffmann-LaRoche Ltd. v. Canada (Commissioner of Patents)*, [1955] S.C.R. 414, 23 C.P.R. 1 [*Hoffmann-LaRoche 1955* cited to S.C.R.] for this submission.

[577] I acknowledge that the *Hoffmann-LaRoche 1955* decision does appear to support Apotex's position. *Hoffmann-LaRoche 1955* involved an application for a patent that claimed a new process for making a known substance called aldehyde, as well as aldehyde when made by

that process. The Commissioner of Patents granted the claim for the new process for making aldehyde, but not the claim for aldehyde made by that process. The inventor appealed to the Exchequer Court, without success (*Hoffmann-La Roche Ltd. v. Canada (Commissioner of Patents)*(1953), [1954] Ex. C.R. 52, 19 C.P.R. 80), and then to the Supreme Court of Canada, again without success. In his brief reasons for dismissing the appeal, Chief Justice Cartwright, speaking on behalf of four of five of the justices, stated: “There being nothing new about the product, the appellant is not entitled to obtain a patent therefore even on the basis of a process dependent product claim” (*Hoffmann-LaRoche 1955*, above, at p.415). Little analysis is offered in the single page of Chief Justice Cartwright’s reasons.

[578] I admit to having considerable difficulty in understanding how the conclusion in *Hoffmann-LaRoche 1955* can fit with the protection offered by the *Patent Act*. It seems illogical to me that a process for making a substance can be novel and thus patentable but that a claim for the product when made by that process is automatically not patentable. I understand that situations could exist that would invalidate the product-by-process claim. For example (without limitation):

- a product-by-process claim could be challenged on the basis that the substance, when made by the described process, was anticipated or obvious; or

- an earlier patent or disclosure is to the product made by any means (although, of course, this could not have happened with the '380 Patent since, at that time, *per se* claims were not permitted).

However, where the substance is only claimed when made by a particular process and where the making of the product by that particular process is novel, the boundaries of the claim are well delineated. I cannot see why the claim would automatically be invalidated simply because someone else has claimed the same product made by a different process.

[579] Finally, I observe that the Supreme Court in *Hoffmann-LaRoche 1955* implicitly accepted the validity of the claims to "a new and useful process for manufacture of an aldehyde". There is, in my view, no principled reason why, if the product-by-process claim is invalidated, the new process for making the known substance is not also invalid.

[580] There has been little jurisprudence in which the principle in *Hoffmann-LaRoche 1955*. However, what little there has been over the last 65 years does not, it seems, directly contradict the Supreme Court decision. *Hoffmann-LaRoche 1955* was recently considered by the Federal Court of Appeal in *Abbott Laboratories v. Canada (Minister of Health)*, 2007 FCA 153, 59 C.P.R. (4th) 30 (*Abbott Clarithromycin (FCA)*), where Justice Sharlow observed at paragraph 15 that, "There is no jurisprudence that casts any doubt on the correctness of the principle stated in *Hoffmann.*"

[581] The Court of Appeal also had occasion to examine the applicability of *Hoffmann-LaRoche 1955* in *Bayer AG v. Apotex Inc.*, 2001 FCA 263, 14 C.P.R. (4th) 263 [*Bayer Ciproflaxin*]. In that case, Apotex Inc. appealed from an order prohibiting the Minister of National Health and Welfare from issuing to it an NOC under the *Regulations*. Apotex alleged that Bayer's Canadian patents for ciprofloxacin were invalid because Bayer had already applied

in another country for a patent on the same drug. The inventions were substantially the same but used a different synthesis process. Apotex Inc. relied on *Hoffmann-LaRoche 1955* for the proposition that the differences in the process for the making of the drug were not “legally relevant” (*Bayer Ciproflaxin*, above, at para. 15). In rejecting this argument, Justice Evans, speaking for the Court, commented as follows (*Bayer Ciproflaxin*, above, at para. 16):

> In our view, however, that case is readily distinguishable from the case at bar. In particular, the issue in Hoffmann-La Roche, supra, was whether the patent application satisfied the requirement in paragraph 28(1)(b) of the Patent Act that a patent may only be obtained for an invention to the extent that it contains an element of novelty. This is not the question before us. What we must decide is whether the inventions that are the subject of the Chilean and Canadian patents are the same invention. And, as counsel for Bayer points out in his memorandum, Apotex did not allege in any of its notices of allegations that the product by process patent obtained in Canada for ciprofloxacin was invalid because ciprofloxacin had already been invented, and that the use of the malonic ester synthesis process to produce an intermediate could not therefore render the invention novel. [Emphasis added.]

[582] In summary, it appears that I must accept the holding of *Hoffmann-LaRoche 1955*. In contrast to the situation before Justice Evans in *Bayer Ciproflaxin*, Apotex has clearly argued that the product-by-process claims are invalid because the substance – lovastatin or Monacolin K – had already been invented. Paraphrasing the words of Justice Sharlow in *Abbott Clarithromycin (FCA),* above, for the purposes of applying the *Hoffmann-LaRoche 1955* principle, lovastatin is "known" as of June 15, 1979, if a hypothetical claim for its invention would fail on the ground of anticipation or lack of novelty.

[583] Apotex submits that the existence of Red Yeast Rice – a substance known for centuries – would satisfy this test. The issue is whether the product lovastatin, as described in the '380 Patent, however made, was anticipated by Red Yeast Rice.

(d) *Evidence of lovastatin in Red Yeast Rice prior to the priority date*

[584] The first question is whether the evidence before me establishes that Red Yeast Rice was a source of lovastatin before the priority date. If it does not, then the claim of anticipation must fail. However, if I am persuaded that, on a balance of probabilities, Red Yeast Rice, prepared by traditional methods, contained lovastatin, I will continue on to consider whether there was both disclosure and enablement.

[585] In Dr. Harding's opinion, there is ample scientific literature that indicates that Red Yeast Rice and similar products "produced in solid phase fermentation and using strains of *Monascus* that were traditionally employed, have appreciable levels of Monacolin K [lovastatin] and are effective in lowering blood cholesterol *in vivo*" (Harding Expert Report, Exhibit 115, para. 52). Dr. Harding concludes that, "people have consumed Monacolin K for centuries."

[586] Dr. Harding stated that the amount of Monacolin K in Red Yeast Rice will vary depending on the fermentation conditions used. It follows (and Dr. Harding did not disagree) that not all Red Yeast Rice contains Monacolin K.

[587] In addition to his literature search, Dr. Harding tested two different samples of Red Yeast Rice products that he bought from Asian specialty markets in Winnipeg and Toronto. His conclusion was that both samples contained low, but detectable, levels of Monacolin K.

[588] I will begin with the results from Dr. Harding's tests on two commercial samples of Red Yeast Rice. Even if those samples did contain measurable quantities of lovastatin (Monacolin K) (which I am prepared to accept), these samples were produced well after the priority date of the invention of the '380 Patent. They tell us nothing about the existence of lovastatin in Red Yeast Rice at any time prior to 1979. Moreover, beyond representations on the packaging, we have no evidence as to how these commercial products were produced and whether the lovastatin found in the samples resulted from traditional methods of fermentation.

[589] As described by Dr. Harding, the modern techniques of producing Red Yeast Rice would differ from traditional methods:

> The modern techniques would employ things like flasks and control environments. Traditionally these things were fermented in boxes or bamboo plates, containers, in open areas, and the temperature was controlled either by fanning or ensuring no direct sunlight, these sorts of things, but also by mixing the rice to uniformly distribute the yeast to get the full colour and the final product through every kernel of rice, but it's also to reduce the temperature.

[590] In his Expert Report, Dr. Harding also notes that, while traditional and modern production practices are quite similar, "modifications [have] been introduced into modern production to enhance the production of the desired metabolites" (Harding Expert Report, Exhibit 115, para. 28).

[591] Dr. Havel, an expert presented to the Court by Merck, also commented that:

> Samples collected in January to April 1998, 12 years after the Negishi paper, may have been produced under conditions which were not, I believe, we can consider truly traditional red yeast rice on or before 1980.

[592] In my view, Dr. Harding's opinion that the two samples he tested were prepared in accordance with traditional methods is speculative. The results of Dr. Harding's tests on two Red Yeast Rice samples cannot be used to reliably demonstrate that, before the priority date, Red Yeast Rice contained lovastatin.

[593] I have similar difficulties with the literature referenced by Dr. Harding in his Expert Report. One article was cited as Negishi et al, "Productivity of Monacolin K in the genus Monascus species" (referred to as Negishi). Negishi reports having tested 124 *Monascus* strains in total. Almost all of the species were isolated from several different red yeast food products. Negishi used modern techniques to carry out the experiments, and found that 17 strains of five species were capable of producing Monacolin K. The initial problem that I have with this paper is that it post-dates, by many years, the priority date of the '380 Patent. I have no information on how the Red Yeast Rice samples were collected and whether these same products would have been available in the years before 1979.

[594] Another reference by Dr. Harding was a 2001 journal article by Heber et al, entitled "An Analysis of Nine Proprietary Chinese Red Yeast Rice Dietary Supplements: Implications of Variability in Chemical Profile and Contents" (referred to as Heber). Heber purchased nine different commercially available dietary Red Yeast Rice supplements and found total Monacolin

K content from 0% to 0.58%. While the paper may demonstrate that a few samples of Red Yeast Rice products collected and tested for purposes of the paper contained measurable amounts of Monacolin K, they do not establish that lovastatin existed in Red Yeast Rice prior to 1979.

[595] The only possible link between testing that occurred after 1979 and the potential for the production of lovastatin from Red Yeast Rice prior to that date would be the production methods. Dr. Harding appears to base his overall opinion that traditional Red Yeast Rice has contained Monacolin K throughout the centuries on the observed similarities between traditional and modern production methods. If it can be established that the production methods used in both periods were the same, it may be possible to extrapolate post-1979 results to pre-1979 samples of Red Yeast Rice.

[596] Dr. Harding testified in cross-examination that, of the seven pieces of prior art cited in his report, only two dealt with the fermentation of Red Yeast Rice prior to 1979.

[597] However, upon closer examination, there were significant differences in the traditional methods of producing Red Yeast Rice and those that would produce lovastatin, including:

- traditional Red Yeast Rice was most likely be fermented at temperatures in excess of 30ºC where lovastatin cannot be produced;

- there is an inverse relationship between the amount of pigment-producing ability and the amount of lovastatin-producing ability in Red Yeast Rice; and

- the modern strains of Red Yeast Rice provide no information about whether the traditional Red Yeast Rice produced lovastatin.

The evidence is strong that the production of lovastatin is very dependent on the temperature of fermentation. Although Negishi reported that 17 of 50 samples of the *Monascus* species produced Monacolin K, they also reported that Monacolin K was produced only when the fungi were grown at 25ºC. As observed by Negishi, "under conditions of incubation at 30 to 37ºC, those Monacolin K-producing strains lost their capability of producing Monacolin K . . .". The '380 Patent teaches the reader to incubate the *A. terreus* fungus at 28°C, a temperature at which *Monascus* would likely be incapable of producing lovastatin.

[598] In sum, I am not persuaded that the evidence demonstrates that lovastatin was contained in Red Yeast Rice prior to the priority date. It follows that Apotex has not satisfied its burden of demonstrating that Red Yeast Rice anticipates lovastatin.

(e) *Disclosure of lovastatin in Red Yeast Rice*

[599] In the event that I am wrong in this conclusion, I will assume that lovastatin was contained in at least some samples of Red Yeast Rice prior to the relevant date. The question is whether this satisfies the requirement of disclosure. In my view, as discussed in the following, Apotex has not persuaded me that the subject matter of the invention - lovastatin – was disclosed to the public by Red Yeast Rice.

[600] The evidence demonstrates that, if Red Yeast Rice contained lovastatin, it did not do so under all conditions of fermentation. That is, prior to June 15, 1979, not every Red Yeast Rice product contained lovastatin. Further, it is also evident that persons who produced or used Red Yeast Rice were unaware that it contained lovastatin.

[601] Apotex argues that *Calgon Carbon Corp. v. North Bay (City)*, 2008 FCA 81, 64 C.P.R. (4th) 337 at paragraph 8 and *Baker Petrolite Corp. v. Canwell Enviro-Industries Ltd.*, 2002 FCA 158, 17 C.P.R. (4th) 478 at paragraphs 35, 42 [*Baker Petolite*] stand for the proposition that the extent or duration of the prior use or sale is not important; that disclosure to "even one member of the public" destroys the novelty of a chemical product. Thus, Apotex submits, the existence of lovastatin, in even one sample of Red Yeast Rice, as of the priority date would be anticipatory of the compound claimed in the '380 Patent.

[602] I disagree with Apotex's assertion that the existence of lovastatin in even one sample of Red Yeast Rice is sufficient to demonstrate disclosure. I think that Apotex confuses "disclosure to one member of the public" as stated in *Baker Petrolite*, above, at paragraph 42, with "one disclosure". If the prior art invariably or predictably discloses the compound, there may well be anticipation. However, where the existence of the compound alleged to be anticipatory cannot be reasonably or consistently predicted from a large universe of possibilities, I cannot see how this could possibly meet the test for disclosure. Anticipation must be more than an accidental presence of a compound.

[603] Not only does Apotex's argument appear illogical to me, it is not supported by the jurisprudence. In *Abbott Clarithromycin* (*FCA*), above, at paragraph 22, the Court of Appeal considered the argument of Abbott that a skilled person must have certain knowledge regarding the prior art.

> Abbott argues that a person skilled in the art who heated clarithromycin Form I by the known technique would not and could not know that clarithromycin Form II had been created, unless they also knew that the heating process had to be stopped before the substance reached its melting point at 225ºC. In my view, the absence of that knowledge is legally irrelevant. The undisputed evidence is that clarithromycin Form II would have been present if the heating technique had been followed. There were well established analytical techniques that would have disclosed its presence if anyone had cared to look at the appropriate moment. [Emphasis added.]

[604] In the case before me, I have no such evidence that lovastatin would have been present in Red Yeast Rice. Indeed the evidence, as disclosed in the literature cited (for example, Negishi and Heber), is that lovastatin was present only in a very few samples.

[605] Apotex also argues that the fact that no one, including the skilled person, ever recognized that Red Yeast Rice contained lovastatin is not relevant. Apotex submits that the Federal Court of Appeal, in *Abbott Laboratories v. Canada (Minister of Health)*, 2006 FCA 187, 56 C.P.R. (4th) 387 at paragraphs 15-23, refers to the principle, outlined by Lord Hoffmann in *BV v. Smithkline Beecham plc*, [2005] UKHL 59, [2006] 1 All ER 685 [*Synthon BV*], that a patent is disclosed even though the author or maker of the prior art was not aware that he was doing so. Apotex refers to *Synthon BV*, above, at paragraphs 22-23 for support on this point.

[606] I agree with Apotex that the cited passage of the House of Lords decision in *Synthon BV*, above, does contain a reference to the fact that an awareness of infringement is not a requirement. However, an examination of the entire passage clarifies the context in which those remarks were made. As stated by Lord Hoffmann in *Synthon BV*, above, at paragraphs 22-23:

> . . . the matter relied upon as prior art must disclose subject matter which, if performed, would necessarily result in an infringement of the patent. . . . But patent infringement does not require that one should be aware that one is infringing: "whether or not a person is working [an] ... invention is an objective fact independent of what he knows or thinks about what he is doing": *Merrell Dow Pharmaceuticals Inc v H N Norton & Co Ltd* [1996] RPC 76, 90. It follows that, whether or not it would be apparent to anyone at the time, whenever subject-matter described in the prior disclosure is capable of being performed and is such that, if performed, it must result in the patent being infringed, the disclosure condition is satisfied. The flag has been planted, even though the author or maker of the prior art was not aware that he was doing so.
>
> Thus, in *Merrell Dow*, the ingestion of terfenadine by hay-fever sufferers, which was the subject of prior disclosure, necessarily entailed the making of the patented acid metabolite in their livers. It was therefore an anticipation of the acid metabolite, even though no one was aware that it was being made or even that it existed. But the infringement must be not merely a possible or even likely consequence of performing the invention disclosed by the prior disclosure. It must be necessarily entailed. If there is more than one possible consequence, one cannot say that performing the disclosed invention will infringe. The flag has not been planted on the patented invention, although a person performing the invention disclosed by the prior art may carry it there by accident or (if he is aware of the patented invention) by design. Indeed, it may be obvious to do so. But the prior disclosure must be construed as it would have been understood by the skilled person at the date of the disclosure and not in the light of the subsequent patent. As the Technical Board of Appeal said in *T/396/89 UNION CARBIDE/high tear strength polymers* [1992] EPOR 312 at para 4.4:
>
> > "It may be easy, given a knowledge of a later invention, to select from the general teachings of a prior art document certain conditions, and apply them to an example in that document, so as to

> produce an end result having all the features of the later claim. However, success in so doing does not prove that the result was *inevitable*. All that it demonstrates is that, given knowledge of the later invention, the earlier teaching is capable of being adapted to give the same result. Such an adaptation cannot be used to attack the novelty of a later patent."

[607] An understanding of this passage demonstrates that Apotex has selectively read the comments of Lord Hoffmann, omitting a key consideration. I agree with Apotex that an awareness that the prior art discloses the anticipatory invention is not a requirement of disclosure. Justice Hughes made that point in *Abbott Clarithromycin (FC)*, above, at paragraph 75. However, while supporting the argument of Apotex, the passage from *Synthon BV*, above, makes it very clear that the disclosure requirement is only met where infringement must occur when the prior art is practised. Paraphrasing the words of Lord Hoffmann, the flag of anticipatory disclosure is not planted on the patent in question unless the prior disclosure would necessarily result in an infringement of the patent.

[608] Applied to the situation before me, Red Yeast Rice only satisfies the disclosure requirement of the test for anticipation if it can be said to necessarily produce lovastatin. As we know from the evidence, that is definitely not the case. Indeed, the evidence before me is that the existence of lovastatin in Red Yeast Rice would be a very rare event.

[609] In conclusion on this issue, I do not accept Apotex's submission that lovastatin was anticipated by Red Yeast Rice.

XI. Conclusion

[610] As noted at the beginning of these reasons, this litigation was subject to the Bifurcation Order. Thus, the matter proceeded to trial without requiring the parties to adduce evidence at trial on any issue of fact pertaining to the following:

1. the extent of infringement, if any, by the Defendants of the ‘380 Patent;

2. the amount of damages suffered, if any, by the Plaintiffs as a result of any such infringement; or

3. the amount of profits earned by the Defendants from any such infringement.

[611] According to the terms of the Bifurcation Order, the determination of whether the Plaintiffs are entitled to elect to recover profits was to be determined by the trial judge. In final arguments, Merck submitted that it wished to elect to recover profits. Apotex objected.

A. *Damages or Profits*

[612] Once a patentee has successfully demonstrated infringement, the Court has the discretion to grant the patentee's choice of remedies – either damages (pursuant to s. 55 of the *Patent Act*) or an accounting of profits (pursuant to s. 57 of the *Patent Act*). Merck wishes to elect an

accounting of profits and asks this Court to so direct. Apotex argues that I should not exercise my discretion in this case.

[613] While both damages and accounting of profits are intended to provide compensation to a wronged plaintiff, the fundamental principles underlying the two remedies and the practical considerations are substantially different.

[614] The object of an award of damages is to make good any loss suffered by the plaintiff as a result of the defendant's infringement of the patent. Quantification of the award is based on the losses suffered by the plaintiff; any gains realized by the defendant because of its wrongdoing are not relevant. On the other hand, an accounting of profits is based on the premise that the defendant, by reason of its wrongful conduct, has improperly received profits which belong to the plaintiff. The objective of the award is to restore those actual profits to their rightful owner, the plaintiff, thereby eliminating whatever unjust enrichment has been procured by the defendant. Calculation is based on the profits wrongfully gained by the defendant; any other losses suffered by the plaintiff are irrelevant.

[615] An accounting of profits is not an easy calculation. As was stated by the late Justice Paul Rouleau, of this Court, when speaking about such an accounting in *Beloit Canada Ltd. v. Valmet-Oy.* (1993), 55 C.P.R. (3d) 433 at para. 3, [1994] F.C.J. No. 682 (F.C.T.D.)(QL), rev'd in part 61 C.P.R. (3d) 271, [1995] F.C.J. No. 733 (QL)(F.C.A.), leave to appeal to S.C.C. refused, [1995] S.C.C.A. No. 388 (QL), 64 C.P.R. (3d) vi:

> This was undoubtedly a most expensive, lengthy and difficult reference and one which clearly underlines the pitfalls of granting

> the remedy of an accounting of profits other than in exceptional and appropriate circumstances and after due deliberation by the court.

[616] In spite of practical difficulties, the Federal Court of Appeal in *Beloit Canada Ltd. v. Valmet Oy* (1992), 45 C.P.R. (3d) 116 at para. 10, [1992] F.C.J. No. 825 (QL), stated that it could:

> ...see no reason in principle why a patentee, whose property has been wrongly appropriated through infringement, should not recover all the profits, direct and indirect, derived by the infringer from his wrongful infringement.

[617] It is necessary for a party seeking an equitable remedy, such as profits, to show some basis for the exercise of equity (*Janssen-Ortho Inc. v. Novopharm Ltd.*, 2006 FC 1234, 57 C.P.R. (4^{th}) 58 at para. 132, aff'd 2007 FCA 217, 59 C.P.R. (4^{th}) 116 leave to appeal to S.C.C. refused, [2007] S.C.C.A. No. 442 (QL), 383 N.R. 397 (note); *Servier FC*, above, at para. 507).

[618] Merck submits that it can demonstrate a basis for an election of profits. Specifically, it puts forward the following factors:

- The Plaintiffs have not committed any inequitable conduct which would disentitle them to equitable relief.

- The Plaintiffs did not delay in commencing the litigation. The infringement action was commenced on June 12, 1997, within 3 months of Apotex Inc. receiving an NOC for Apo-lovastatin.

- The Defendants could not have doubted that the Plaintiffs would pursue an infringement action given the lengthy history of prior lovastatin litigation.

- The reasons why the litigation took years to prosecute are not, Merck submits, reasons to disentitle the Plaintiffs to equitable relief:

    - the long and complicated facts of the cases: we are dealing with a process patent, where the acts of infringement are conducted in secret, requiring the Plaintiffs to attempt to prove infringement through a long discovery process and repeated motions for productions;

    - AFI's history of use of *Aspergillus terreus* to make lovastatin going back to 1991 to 1999;

    - the transfer of *Aspergillus terreus* and AFI-1 technology to Blue Treasure in 1995 and its use;

    - the filing of a statement of claim in T-1169-01;
    - Apotex Inc.'s refusal to agree to consolidate the two proceedings for discovery meaning that the Plaintiffs had to repeat to a large extent the discovery from the infringement action;

- the patent expiry on January 31, 2001, thereby capping the period of infringement as of that date; and

- two years of the delay due to the length of the trial requested.

- Delay in the action is a factor that is more related to the complicated facts of the proceeding rather than the diligence of the Plaintiffs.

[619] While I agree with Merck that it has not committed any inequitable conduct that would disentitle them from the equitable remedy of profits, other factors weigh against such a remedy in this case.

[620] A factor that causes me serious concern is the time that this matter took to come to trial. Merck attempts to distance itself from any decisions that resulted in the delay of this trial for almost thirteen years. I cannot accept that the Defendants and the Federal Court bear all of the responsibility for the delay. The consequence of this delay is, inevitably, that reaching back to the period between 1997 and 2001 to assess Apotex profits would be exceedingly difficult.

[621] The difficulty in assessing profits is further exacerbated by the complexities of the commercial arrangements that involved not only AFI and Apotex Inc., but also Blue Treasure and Biogal. Merck consented to the settlement involving Biogal’s interests on May 28, 2010.

[622] An additional layer of complexity comes from the fact that Merck does not assert that all of the lovastatin that was produced during the 1997 to 2001 period infringed the '380 Patent. On the Canadian-produced material by AFI, except for the batch referred to as CR0157, there is no assertion of infringement. I have also concluded that Merck has not made out its case for infringement with respect to all of the Blue Treasure productions.

[623] Dissecting Apotex's profits to account for the Biogal settlement and the non-infringing production would be a complex undertaking.

[624] Balancing the factors in this case, I am not persuaded that I ought to exercise my discretion and permit the Plaintiffs to elect an accounting of profits. The Plaintiffs will be entitled to their damages. Specifically, a hearing under ss. 107 and/or 153 of the *Federal Courts Rules*, SOR/98-106 [*Federal Courts Rules*] shall be conducted to determine: the extent of infringement by the Defendants of the '380 Patent; and, the amount of damages suffered by the Plaintiffs as a result of such infringement.

B. *Exemptions from Liability*

[625] Related to the issue of damages is the question of whether any volumes of lovastatin produced by Apotex should be exempt from a finding of infringement. Apotex relies on s. 55.2(1) of the *Patent Act* (post October 1, 1989) to submit that it should not be held liable for any infringement relating to its experimental and regulatory uses of lovastatin.

[626] Exemptions from liability are founded in s. 55.2(1) of the *Patent Act* (post October 1, 1989). That provision states that:

55.2(1) It is not an infringement of a patent for any person to make, construct, use or sell the patented invention solely for uses reasonably related to the development and submission of information required under any law of Canada, a province or a country other than Canada that regulates the manufacture, construction, use or sale of any product	55.2(1) Il n'y a pas contrefaçon de brevet lorsque l'utilisation, la fabrication, la construction ou la vente d'une invention brevetée se justifie dans la seule mesure nécessaire à la préparation et à la production du dossier d'information qu'oblige à fournir une loi fédérale, provinciale ou étrangère réglementant la fabrication, la construction, l'utilisation ou la vente d'un produit.

[627] Apotex may claim an exemption from liability for certain amounts of the infringing product, provided that it can satisfy its burden to demonstrate that the product was used for permitted purposes (such as obtaining regulatory approval or to comply with regulations) (*Merck & Co. v. Apotex Inc.*, 2006 FC 524, 53 C.P.R. (4th) 1, rev'd on other grounds 2006 FCA 323, 55 C.P.R. (4th) 1 leave to appeal to S.C.C. refused, [2006] S.C.C.A. No. 507 (QL), 370 N.R. 400 (note)).

[628] The Canadian *Food and Drug Regulations*, C.R.C. 1978, c. 869 [*Food and Drug Regulations*], and the United States *Food Drug and Cosmetic Act*, 21 U.S.C., as amended [*Food Drug and Cosmetic Act*], required Apotex Inc. to retain and test samples of lovastatin on a routine basis. Apotex submits that its testing and retention of lovastatin falls within the scope of subsection 55.2(1) of the *Patent Act* and the common law exception and is therefore exempt from infringement.

[629] Apotex submits that the evidence clearly shows that, as required by the Canadian *Food and Drug Regulations*, above, and the regulations under the U.S. *Food Drug and Cosmetic Act*, above, Apotex: (i) acquired and used bulk lovastatin, and formulations incorporating bulk lovastatin, for the purpose of obtaining permission to sell lovastatin containing pharmaceutical products in Canada and the United States; (ii) carried out in process quality control sampling of lovastatin formulations; and (iii) retained samples of bulk and finished dosage forms of lovastatin.

[630] Mr. Barber, the Manager of the Formulations Department at Apotex Inc., and Ms. Copsey, Manager of Packaging and Director of Commercial Lab Operations at Apotex Inc., explained in detail how Apotex Inc. used lovastatin for these purposes. The business records of Apotex Inc. adduced at trial reflect those uses. Apotex submits that its use of lovastatin for these experimental and regulatory purposes is exempt from infringement under s. 55.2(1) and (6) of the *Patent Act* (post October-1989) and the common law.

[631] Mr. Fahner was the Vice-President of Finance at Apotex Inc. during the relevant times. He compiled charts identifying the quantities of lovastatin from each lot of bulk lovastatin and finished dosage batch that were used by Apotex Inc. for each of the purposes described by Mr. Barber and by Ms Copsey, namely, the research and development work in preparation of the submission batches, the retention of API samples and the process sampling and finished goods retention. Apotex Inc. submits that the evidence establishes that the following quantities of

lovastatin were used by Apotex Inc. for regulatory and experimental purposes and should be exempt from any finding of infringement:

Use of lovastatin by Apotex Inc.	Total Quantity (in kg)
Research and Development	59.1111
Reserve Samples (API)	22.0986
In Process Samples	6.58078
Finished Goods Retained Samples	4.2654

[632] I do not understand Merck to be objecting to the exemption of these Apotex Inc. volumes from a finding of infringement. I am satisfied that the volumes set out in the above table are exempt from any finding of infringement.

[633] AFI also conducted research and development work involving the use of the micro-organism *Aspergillus terreus* after the assets of ABI were acquired in July 1991. Initially, the work was a continuation of the work commenced by ABI in 1988 and was specifically related to obtaining a compulsory licence. Subsequently, the work involved the research and development of *Aspergillus terreus* for regulatory submissions and for eventual commercialization of *Aspergillus terreus* lovastatin. In the course of these activities, ABI, and subsequently AFI, manufactured 6.9 kg of *Aspergillus terreus* lovastatin. This was supplied to Apotex Inc. and used for research and development purposes and for regulatory submissions. AFI submits that this work is exempt from infringement. I agree.

[634] In 1998 and 1999, AFI ran a few fermentations using *Aspergillus terreus* at the 14,000 litre scale for research and development purposes directed to market readiness upon expiry of the '380 Patent. A total of 13.45 kg was manufactured from these runs. The Defendants assert that this work is exempt from infringement. In June 2002, this material was supplied to Brantford

Chemical Inc., a sister company to Apotex Inc., for development purposes in an effort to make simvastatin, another statin that is not the subject of this litigation. Apotex Inc. submits that there was no evidence at trial that the 13.45 kg was ever used to manufacture tablets for sale in Canada, or elsewhere. This work is exempt from infringement. I agree.

[635] Merck objects to an exemption from liability for any amounts of AFI-1 lovastatin made in Winnipeg during the period 1993 to 1999. In their view, these volumes clearly infringed the '380 Patent. Moreover, through the transfer of the AFI-1 technology to Blue Treasure for commercial purposes, the infringement resulted in a loss of Merck's right to the "full enjoyment of the monopoly" (*Monsanto*, above, at para. 34). Accordingly, Merck argues, these volumes should not be the subject of any "fair dealing" exemption. In addition, Merck submits that the liability should extend to all 296.6 kg of AFI-1 lovastatin that were allegedly made by Blue Treasure.

[636] I am not prepared to make this link. In light of the Supreme Court of Canada's decision in *Micro Chemicals Limited v. Smith Kline & French Inter-American Corp*., [1972] S.C.R. 506, 2 C.P.R. (2d) 193 [*Micro Chemicals*], Merck's allegation is without foundation. In the case at bar, AFI was doing exactly what the defendant did in *Micro Chemicals*. AFI was carrying out research for the purposes of improving its *Aspergillus terreus* process to ensure that the process could be used on a commercial scale. This is the type of activity that the Supreme Court held was exempt from infringement. The supply of the developed technology to Blue Treasure, who was permitted to utilize the AFI-1 process to make lovastatin for sale outside Canada, was not, in the circumstances, an act of infringement.

[637] In sum, I am satisfied that neither the 6.9 kg nor the 13.45 kg of *Aspergillus terreus* lovastatin referred to above should attract liability. Moreover, I am not prepared to conclude that the alleged 296.6 kg of AFI-1 lovastatin that was made using the transferred AFI-1 technology infringed the '380 Patent.

C. *Conclusion*

[638] In conclusion, the action of the Plaintiffs will succeed, in part, and they will be entitled to an order for the recovery of damages sustained as a consequence of the Defendants' infringement of the '380 Patent by the following:

1. all Apo-lovastatin product that was produced by AFI from AFI batch CR0157; and

2. the 294 batches of lovastatin produced by Blue Treasure in China after March 1998 and imported into Canada.

[639] Damages and the extent of infringement will be determined by way of a reference pursuant to Rule 153 of the *Federal Courts Rules* and in accordance with the Bifurcation Order dated November 14, 2003. The parties will be permitted to address the specific terms of a reference as to damages, by way of written submissions to be served and filed within 60 days of the date of the Judgment. The parties will have a further 15 days to serve and file reply submissions.

[640] Merck will also be entitled to an order for prejudgment interest pursuant to ss. 36 and 37 of the *Federal Courts Act*, S.C. 2002, c. 8.

[641] The counterclaims of the Defendants will be dismissed. Specifically, I conclude that the '380 Patent was valid and that Merck & Co. has standing to bring this action.

[642] The question of costs was not addressed by the parties in their final submissions. Obviously, Merck, as the successful party will be entitled to costs, although the amount of those costs should reflect the specific circumstances of this trial. The parties will be given a period of time to attempt to resolve the issue of costs among themselves. I sincerely hope that the direction of this Court is not required. However, in the event that the parties cannot agree on costs, they may serve and file submissions, not to exceed ten pages in length, within 60 days of the date of the Judgment. The parties will have a further 15 days to serve a reply, any such reply not to exceed five pages.

POSTSCRIPT

[1] These Reasons for Judgment are un-redacted from confidential Reasons for Judgment which were issued on December 9, 2010 pursuant to the Direction dated December 9, 2010.

[2] The Court canvassed counsel for the parties whether they had concerns if the reasons were issued to the public without redactions. On December 15, 2010 and December 17, 2010, in separate letters, the parties advised that there are no portions of the confidential Reasons for Judgment that should be redacted.

"Judith A. Snider"
Judge

Ottawa, Ontario
Public Reasons – December 22, 2010
Confidential Reasons - December 9, 2010

Appendix A – List of Witnesses

I. List of Witnesses

A. *Plaintiffs' Expert Witnesses*

(1) Dr. Jerry Lee **Atwood**

Dr. Atwood is a professor and Chairman of the Department of Chemistry at the University of Missouri-Columbia. He obtained a Ph.D from the University of Illinois. Dr. Atwood has been the editor of several scientific publications and has published more than 640 articles in refereed journals. Dr. Atwood was qualified as an expert in organic chemistry.

On behalf of Merck, Dr. Atwood opined on issues of validity. He also compared the chemical characteristics of Compound I in the '380 Patent to the chemical characteristics of Monacolin K in the '794 Patent. Dr. Atwood responded to certain opinions expressed Dr. Robert McClelland in his Expert Report.

(2) Mr. Robert Hubbell **Barriga**r

Mr. Barrigar is a barrister and solicitor and a registered Canadian patent agent. He obtained an LL.M Degree from Harvard Law School. He has practised in intellectual property law for 30 years. His practice involved litigation pursuant to s. 45(8) of the “old” Patent Act, including patent applications that were the subject of conflict proceedings. Mr. Barrigar was qualified in matters of patent agency and procedures in the Canadian Patent Office, including practices of the Commissioner of Patents at the relevant time.

On behalf of Merck, Mr. Barrigar provided his opinion on whether the ‘380 and ‘794 Patents would have been placed in conflict proceedings by the Canadian Patent Office.

(2) Dr. Jon **Clardy**

Dr. Jon Clardy is a professor at the Harvard Medical School, in the Department of Biological Chemistry and Molecular Pharmacology. He has a Ph.D in Organic Chemistry. Currently, Dr. Clardy holds positions as the Co-Director, Harvard University Program in Chemical Biology; Senior Associate Member, Broad Institute of Harvard and MIT; and the Infectious Disease Initiative, Broad Institute of Harvard and MIT. Dr. Clardy was recognized as an expert in organic chemistry, medicinal chemistry, natural products chemistry, and the biosynthesis of microbial metabolites.

On behalf of Merck, Dr. Clardy opined on the construction and validity of the '380 Patent.

(3) Dr. Julian **Davies**

Dr. Davies is a professor emeritus of Microbiology and Immunology at the University of British Columbia, where he has worked since 1992. Dr. Davies obtained his Ph.D in Organic Chemistry from the University of Nottingham. He was qualified as an expert in the area of microbial genetics and microbiology.

On behalf of Merck, Dr. Davies gave opinion evidence on issues relating to infringement of the '380 Patent. In 2003 and in 2007, samples of raw and processed lovastatin were tested under his supervision for the DNA of *Aspergillus terreus* and *Coniothyrium fuckelii*.

(4) Dr. Antonio Marion **Gotto**

Dr. Gotto is a professor of Medicine at Cornell University. In addition to a Ph.D in Biochemistry from Oxford University, he earned an M.D. from Vanderbilt University. Dr. Gotto was qualified as an expert in the area of atherosclerosis, lipid metabolism and cardiovascular risk protection.

On behalf of Merck, Dr. Gotto gave opinion evidence on cholesterol, cardiovascular disease and the discovery and use of lovostatin.

(5) Dr. Richard **Havel**

Dr. Richard Havel is a physician specializing in medicine, endocrinology and metabolism. Dr. Havel is a professor emeritus at the University of California, and he has served as an editor of the American Journal of Clinical Nutrition. Dr. Havel was qualified as an expert in internal medicine, clinical nutrition, endocrinology and metabolism, specifically the treatment of patients with hyperlipidemia, hypercholesterolemia and cardiovascular disease.

On behalf of Merck, Dr. Havel gave opinion evidence on the issues surrounding red yeast rice and the '380 Patent.

(6) Dr. Linda Lee **Lasure**

Dr. Lasure obtained a Ph.D in Genetics from the University of Syracuse. Dr. Lasure has worked for various pharmaceutical corporations, including as staff scientist at Pacific Northwest National Lab, where she established a new program to apply fungal biotechnology to the problem of efficient conversion of lignocellulosic biomass to commercial products. She has authored numerous papers, chapters and books relating to industrial microbiology and currently holds three patents related to fungal biotechnology. Dr. Lasure was qualified as an expert in industrial microbiology.

On behalf of Merck, Dr. Lasure opined on construction and infringement of the '380 Patent.

(7) Mr. Brian **Lindblom**

Mr. Lindblom is a forensic document examiner and the founding principal of Document Examination Consultants Inc. Mr. Lindblom was qualified as an expert in forensic document examination.

On behalf of Merck, Mr. Lindblom opined on the authenticity of the documents produced by AFI that were alleged to be Blue Treasure's Batch Records.

(8) Dr. Bernard A. **Olsen**

Dr. Olsen obtained a Ph.D in Analytical Chemistry from the University of Wisconsin, and then worked for 29 years as a senior research fellow at Eli Lilly and Company. Currently, Dr. Olsen is an independent pharmaceutical consultant. He was qualified as an expert in the area of analytical chemistry.

On behalf of Merck, Dr. Olsen analyzed 11 test samples of Red Yeast Rice using High-Performance Liquid Chromatography (HPLC). The results were compared to the HPLC results of Compounds I, II, III, and IV of the '380 Patent.

B. *Plaintiffs' Fact Witnesses*

(1) Dr. Alfred **Alberts**

Dr. Alberts is one of the named inventors on the '380 Patent. He testified regarding the invention of lovastatin.

(2) Ms. Rebecca **Gentile** (Gilbert)

Ms. Gentile (formerly Gilbert) is the Senior Stability Coordinator for Merck & Co. Her responsibilities include generating and compiling data for use in regulatory filings. She testified regarding the Red Yeast Rice project at Merck & Co.

(3) Mr. Ronald **Harvey**

Mr. Harvey was the Director of Marketing for Merck Frosst in 1997 (now retired). He testified regarding the marketing procedures used at Merck and the sales figures for lovastatin in 1997.

(4) Mr. Ted **Kavowras**

Mr. Kavowras is the Managing Director of Panoramic Consulting, an investigative business based in Hong Kong. Mr. Kavowras testified that he obtained lovastatin from Blue Treasure between 2000 and 2001.

(5) Ms. Donna **Kugit**

Ms. Kugit, an employee of Merck, testified regarding the samples that were packaged and shipped to Bill Richardson.

(6) Dr. Natalie **Lazarowych**

Dr. Lazarowych is the Chief Scientific Officer and Director of Research at Dalton. In 2003, Dalton did work for law firm McCarthy Tetrault LLP with respect to lovastatin. She testified regarding the preparation of lovastatin samples that were sent to the law firm at that time.

(7) Ms. Carol **Mercer**

Ms. Mercer is an administrative assistant with the IP litigation department at Merck. She testified about Merck's protocol for logging and labeling samples that are put into their database.

(8) Mr. Robert **Quesnel**

Mr. Quesnel is the Vice-President of Legal Affairs & General Counsel for Sanofi Aventis Canada, and was the Director of Legal Affairs at Merck Frosst Canada from 1995 to 2007. He spoke to the legal issues surrounding Apo-lovastatin.

(9) Mr. James P. **Richardson**

Mr. Richardson is the Director of Tax Planning for Merck Sharp and Dohme Corp., and has worked as in some capacity as an accountant for them for over 25 years. He testified regarding the license agreement, dated January 1, 1985, between Merck and Co. Inc. and Merck Frosst Canada.

(10) Ms. Elizabeth Giuliani **Scott**

Ms. Scott was employed as in-house counsel for Merck and Co between 1998 to 2007. She testified that she communicated with, and received samples from, Mr. Kavowras.

C. *Defendants' Expert Witnesses*

(1) Dr. Neal **Connors**

Dr. Connors holds a Ph.D in microbiology from Ohio State University. For 17 years, Dr. Connors was an employee with Merck Research Laboratories, where he worked as a senior research biochemist and a senior investigator focusing on strain development for both fungi and bacteria. Since 2009, Dr. Connors has been the President of Phoenix BioConsulting, LLC, and provides scientific consulting services to the fermentation, industrial microbiology and biotechnology sectors. Dr. Connors was qualified as an expert in industrial microbiology.

On behalf of Apotex, Dr. Connors gave opinion evidence on the AFI-4 *Coniothyrium fuckelii* process for producing lovastatin. He responded to Dr. Lasure's opinion on the AFI-4 process for making lovastatin in commercial quantities during the period commencing April 1996.

(2) Dr. Marcus Thomas Pius **Gilbert**

Dr. Gilbert is an associate professor at the Natural History Museum of Denmark's Centre of GeoGenetics at the University of Copenhagen. He completed a D.Phil in the Department of Zoology at the University of Oxford, where his research focused on ancient DNA analysis. He has written numerous articles on analysis of ancient DNA and also teaches on the subject. Dr. Gilbert was qualified as an expert in the analysis of low copy and degraded DNA.

On behalf of Apotex, Dr. Gilbert opined on infringement, specifically on the issue of ancient DNA. Dr. Gilbert replied to the Expert Report of Dr. Davies and commented on Dr. Davies's experimental results.

(3) Dr. Scott **Harding**

Dr. Harding is an adjunct professor in the Department of Human Nutritional Science and a research associate at the Richardson Centre for Functional Foods and Nutraceuticals at the University of Manitoba. Dr Harding received a Ph.D from McGill University. He was qualified as an expert in human nutrition and metabolism.

On behalf of Apotex, Dr. Harding gave opinion evidence on the Monacolin K producing capabilities of traditional Chinese Red Yeast Rice. In addition, he replied to the Expert Reports of Drs. Havel, Clardy and Oslen.

(4) Mr. Robert **Hirons**

Mr. Hirons is a registered patent agent in Canada with over 40 years of experience. He has been involved in the prosecution of numerous applications before the Commissioner of Patents, several of which involved conflict proceedings. Mr. Hirons was qualified as an expert in Canadian patent prosecution and practice between 1980 and 1982 and knowledgeable about the practices of the Commissioner of Patents at that time.

On behalf of Apotex, Mr. Hirons gave opinion evidence on whether the '380 Patent and the '794 patent should have been placed in conflict proceedings by the Commissioner of Patents. Mr. Hirons also replied to the Expert Report of Mr. Barrigar.

(5) Dr. Robert Allan **McClelland**

Dr. McClelland is professor emeritus in the Department of Chemistry at the University of Toronto. His research focus is biological and medicinal chemistry, and he has received numerous research awards in Canada. Dr. McClelland was qualified as an expert in organic and medicinal chemistry.

On behalf of Apotex, Dr. McClelland opined on the construction and validity of the '380 Patent. Specifically, he compared the chemical characteristics of Monacolin K ('794 Patent) and Compound I ('380 Patent). In addition, Dr. McClelland's report replied to the Expert Report of Dr. Atwood.

(6) Dr. Hendrik Nicholas **Poinar**

Dr. Poinar is an associate professor in the Department of Anthropology at McMaster University. He obtained a Ph.D in molecular evolutionary genetics and biomolecular anthropology from Lüdwici Maximillians Universität München. Dr. Poinar has worked in the field of ancient DNA for more than 15 years and has published 44 peer-reviewed articles on the subject. He is considered one of the founding members of the field of ancient DNA. Dr. Poinar was qualified as an expert in the extraction and characterization of low copy number and degraded DNA.

On behalf of Apotex, Dr. Poinar opined on infringement issues, specifically the experimental results of Dr. Davies. In addition, he was asked to replicate Dr. Davies's finding using similar methods.

(7) Dr. Robert A. **Samson**

Dr. Samson received an M.Sc and Ph.D from the University of Utrecht in the Netherlands. Dr. Samson is the head of the Department of Applied and Industrial Mycology at the CBS Fungal Biodiversity Centre in the Netherlands. His research is focused on polyphasic taxonomy of the fungal genera *Penicillium* and *Aspergillus*. He was qualified as an expert in applied and industrial mycology with specific expertise in the polyphasic taxonomy of the genus *Aspergillus*.

On behalf of Apotex, Dr. Samson opined on the construction of the '380 Patent including the classification of fungal taxonomy. He also responded to the Expert Reports of Dr. Clardy and Dr. Lasure.

(8) Dr. John Lyle **Sorensen**

Dr. Sorensen is an assistant professor in the Department of Chemistry at the University of Manitoba. He obtained a Ph.D in Chemistry from the University of Alberta, where his research focused on the biosynthesis of lovastatin and the pathway used by *Aspergillus terreus*. Dr. Sorensen was qualified as an expert in natural products chemistry.

On behalf of Apotex, Dr. Sorensen opined on construction and validity of the '380 Patent, specifically the fermentation and media conditions contemplated by the '380 Patent. He also replied to the Expert Report of Dr. Clardy.

(9) Dr. John Waldo **Taylor**

Dr. Taylor is a professor in the Department of Plant and Microbial Biology at the University of California at Berkeley. He has studied fungi for 37 years and fungal DNA for 30 years and published more than 160 articles relating to PCR amplification and fungal DNA. Dr. Taylor was qualified as an expert mycologist and microbiologist, with particular expertise in the area of fungal DNA evolution and fungal DNA PCR amplifications.

On behalf of Apotex, Dr. Taylor opined on infringement, specifically in response to the DNA evidence of Dr. Davies.

D. *Defendants' Fact Witnesses*

(1) Mr. Donald **Barber**

Mr. Barber is the Manager of the Formulations Department at Apotex Inc.. He testified regarding the general steps taken in product development at Apotex Inc. and commented on the development of Apo-lovastatin.

(2) Ms. Lori **Christofalos**

Ms. Christofalos is the Manager of Quality Assurance Regulatory Affairs at AFI. She testified about AFI’s standard operating procedures for the fermentation of cultures of *Coniothyrium fuckelii*.

(3) Ms. Elaine **Copsey**

Ms. Copsey has worked for Apotex Inc. since 1999 as Manager of Packaging and Director of Commercial Lab Operations. She testified regarding the procedures for quality control testing at Apotex Inc., specifically the procedures for testing bulk and raw product.

(4) Dr. David **Cox**

Dr. Cox was the President of AFI between 1994 and 1997. On behalf of AFI, he testified about the corporate background of AFI, the *Aspergillus terreus* and *Coniothyrium fuckelii* projects and the technology transfer to Blue Treasure.

(5) Mr. Gordon **Fahner**

Mr. Fahner is the Vice President of Supply Chain and has worked at Apotex Inc. since 1989. He testified regarding the standard operating procedures for Apotex Inc. between 1997 and 2001. Specifically, he spoke about the receipt, storage and use of raw materials.

(6) Mr. Alexander **Fowler**

Mr. Fowler has been the Finance and Administration Manger at AFI since 1996. Mr. Fowler testified regarding the financial matters relating to the technological transfer between AFI and Blue Treasure.

(7) Mr. John **Hems**

Mr. Hems is the Director of Regulatory Affairs at Apotex Inc., where he has worked for 30 years. In his current capacity, Mr. Hems oversees the drug approval submissions to regulatory agencies. He testified that his department was responsible for the regulatory submissions made for Apo-lovastatin in the early 1990s.

(8) Mrs. Qifen **Hu**

Mrs. Hu has been the Manager of the Bacterial Culture Department at Blue Treasure since 1995. She is responsible for receiving and testing cultures received from AFI. Mrs. Hu testified regarding the AFI-4 *Coniothyrium fuckelii* strain and the Blue Treasure batch records.

(9) Mr. Dingjun **Luo**

Mr. Luo has been the Deputy General Manager at Blue Treasure since 1995. He testified regarding the creation, completion and approval of batch records at Blue Treasure. Mr. Luo authored two articles in the Chinese Journal of Antibiotics which describe the production of lovastatin at Blue Treasure. The articles specifically referred to *Aspergillus terreus* as the fungi source.

(10) Mr. Scott **Primrose**

Mr. Primrose has been a senior research scientist with AFI since 1991. He testified regarding the AFI-4 process, specifically the preparation of *Coniothyrium fuckelii* seed banks and the protocols for shipping vials to Blue Treasure.

(11) Dr. Mila **Sailer**

Dr. Sailer has been employed at AFI since 1994 as a natural product chemist and then Director of Technology. Dr. Sailer obtained a Ph.D in experimental mycology at the Institute of Microbiology at the former Czechoslovakia Academy of Science. He was involved in developing the process to create lovastatin from *Coniothyrium fuckelii*. His testimony related to the development of the AFI-4 process, the technology transfer from AFI to Blue Treasure and the differences in optimal fermentation for *Aspergillus terreus* and *Coniothyrium fuckelii*.

(12) Dr. Bernard Charles **Sherman**

Dr. Sherman is the Founder, Executive Chairman, and Chief Executive Officer for Apotex Inc.. He has overall responsibility of the company, but focuses primarily on product development, business development and legal issues. Dr. Sherman testified regarding the formation of AFI, the development of lovastatin and the process of finding a non-infringement method to produce Apo-lovastatin. He also spoke about the joint venture with Blue Treasure.

(13) Dr. Jerry **Su**

Dr. Su worked for AFI from 1996 to 1998 as a fermentation specialist. He was the Group Leader responsible for research and development and the fermentation of AFI-4. Dr. Su spoke about his personal experience visiting Blue Treasure in China and compared their procedures to the procedures at AFI.

E. *Affidavit (March 1, 2010 & April 1, 2010*

(1) Bruce **Davis**

Mr. Davis is currently employed by AFI as QC Production Support Manager and swore in his affidavit that he was asked by Lori Christofalos to send samples to a warehouse in Montreal called Warnex Inc.

(2) Lucinda **Gordon**

Ms. Lucinda Gordon was employed by AFI from August 17, 1992 to September 24, 1998 as a microbiology technician. She swore in her affidavit that on November 3, 1997 she was asked to create an additional *Coniothyrium fuckelii* seed bank at AFI.

(3) Leeyuan **Huang**

Mr. Huang was employed by Merck & Co. Inc as Senior Research Scientist in 1997. He swore in his affidavit that he collected various samples and provided them to Dr. Richard Monaghan of Merck & Co. Inc.

(4) Emily **Malcolm**

Ms. Malcolm is currently a legal assistant at Goodmans LLP and swore in her affidavit that on June 9, 2009 she was given a bag labelled “Red Yeast Rice” and sent it to Taylor McCaffrey LLP in Winnipeg.

(5) Alexander **Patrick**

Mr. Patrick was employed in the summer of 2009 by Goodmans LLP and swore in his affidavit that on June 2, 2009 he purchased a bag of produced labelled “Red Yeast Rice” at Hua Sheng Supermarket located at 293 Spadina Avenue in Toronto.

(6) Angela **Razo**

Ms. Razo is employed as a law clerk by Apotex Inc. and swore in her affidavit that in October 2009 she was asked to collect and send a number of pharmaceutical samples to Dr. Hendrik Poinar at McMaster University in Hamilton.

(7) Heather **Sheps**

Ms. Sheps is currently a legal assistant employed by Taylor McCaffrey LLP and swore in her affidavit regarding the circumstances of the transfer of the Red Yeast Rice product.

(8) Sylvia **Su**

Ms. Su swore in her affidavit that she provided Ms. Lily Su a sample of a packet labelled “yeast” that she obtained from the Triangle Oriental Market located at 748 D East Chatham Street in Cary, North Carolina.

(9) Lee Wen **Su**

Mr. Su was employed as an associate in the law firm of Olsson, Frank and Weeda in 1997. He swore that he delivered samples to Mr. Adams on May 6, 1997.

(10) Yoshikazu **Tani** (Expert Statement)

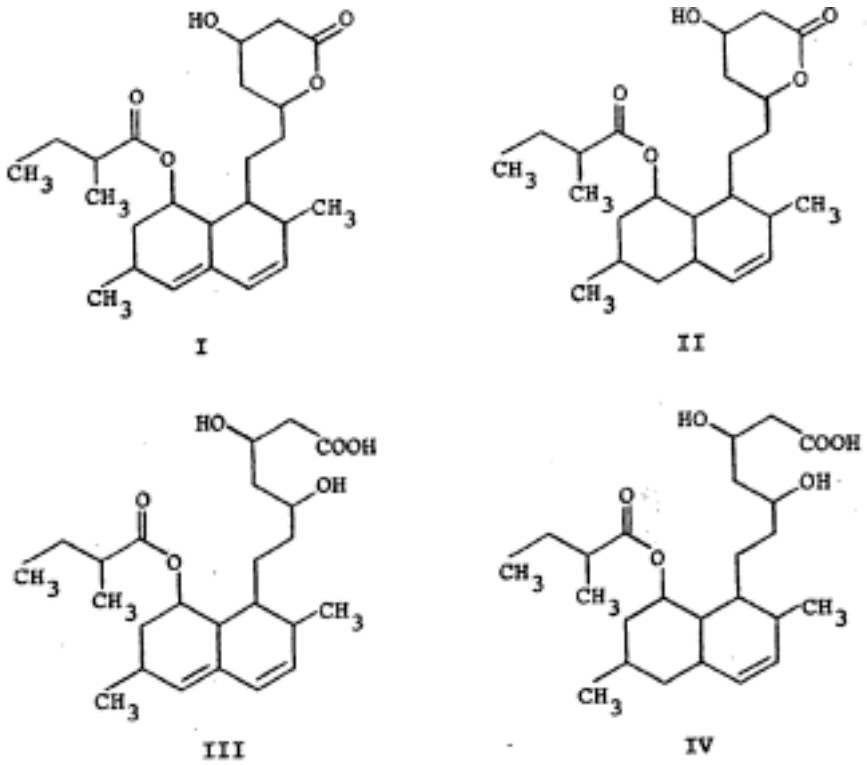
Mr. Tani is a patent attorney and licensed patent agent with the firm of Tani & Abe, located in Tokyo and swore in his affidavit that he was asked by Apotex Inc. to review two documents issued by the Japanese Patent Office related to an invention entitled “Novel Physiologically Active Monacolin K and the Production of Same”.

(11) Xin **Wang**

Ms. Wang is a research technician at the Richardson Centre for Functional Foods and Neutraceuticals and swore in her affidavit that on April 26, 2009 she purchased product labelled “Read Year Rice” at Sun Wah Herb Garden in Winnipeg.

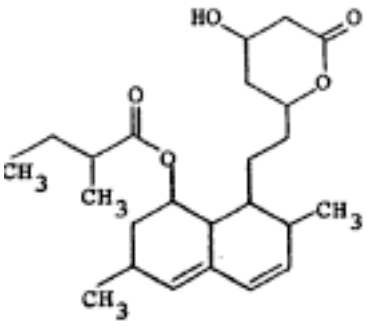
Appendix B – Claims 1 to 8 and 13 to 15 of the '380 Patent

1. A process of producing the compounds of structural formulae:



which compromises fermenting a nutrient medium with a microorganism of the genus *Aspergillus terreus* and isolating the products and when desired converting said products to their corresponding pharmaceutically acceptable salt or lower alkyl ester or a substituted lower alkyl ester wherein the substituent is phenyl, dimethylamine or acetylamine or the cation of the salt is derived from ammonia, ethylenediamine, N-methyl-glucamine, lysine, arginine or ornithine.

2. The process of producing the compounds of structural formulae:



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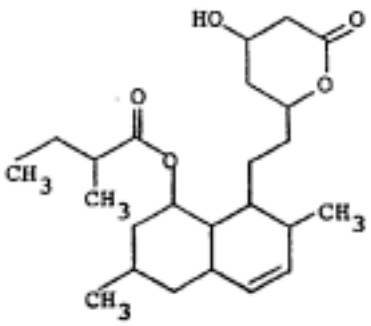


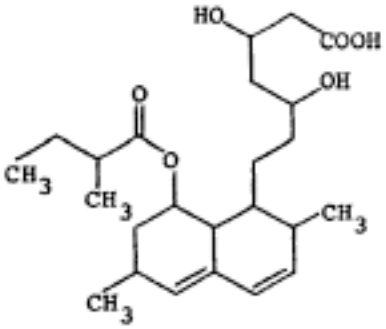
II

which comprises fermenting a nutrient medium with a microorganism of the genus *Aspergillus terreus* and isolating the products.

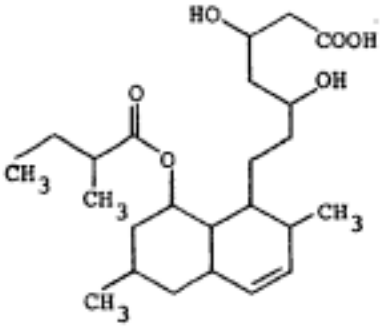
3. The process of Claim 2 in which the microorganism is one deposited in the American Type Culture Collection with Accession number 20541 or 20542.

4. The process of Claim 2 in which the isolation comprises extraction of the fermentation mixture with a solvent followed by chromatography.

5. The process of producing the compounds of structural formulae:



III



IV

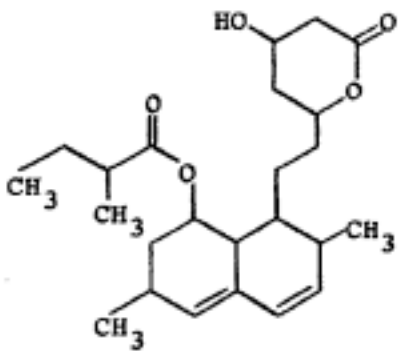
which comprises fermenting a nutrient medium with a microorganism of the genus *Aspergillus terreus* and isolating the products.

6. The process of Claim 5 in which the microorganism is one deposited in the American Type Culture Collection with Accession number 20541 or 20542.

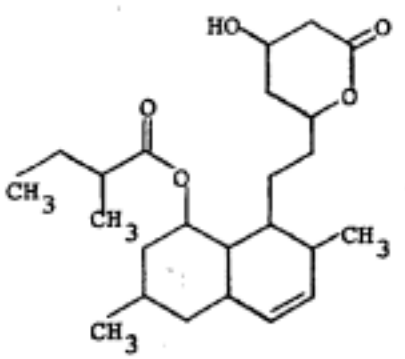
7. The process of Claim 5 in which the isolation comprises extraction of the fermentation mixture with a solvent followed by chromatography.

8. The process of Claim 5, wherein compound III is reacted with ammonia to form the ammonium salt of compound III.

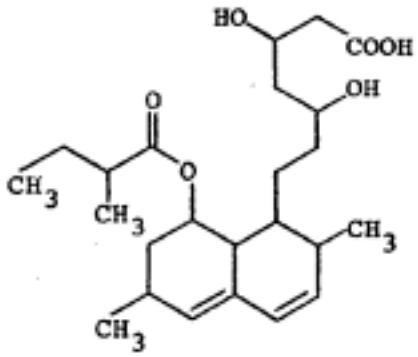
13. A compound selected from:



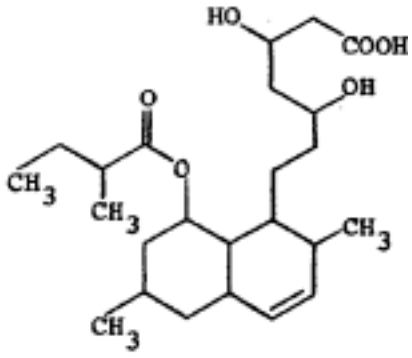
I



II



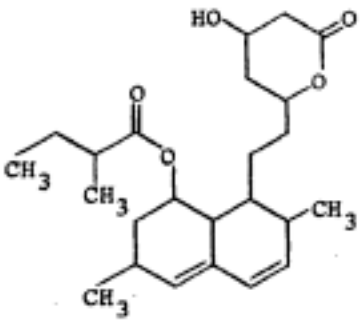
III



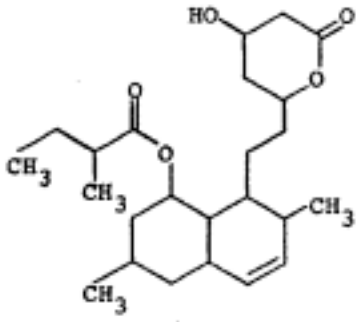
IV

or a pharmaceutically acceptable salt or lower alkyl ester or a substituted lower alkyl ester wherein the substituent is phenyl, dimethylamine or acetylamine or the cation of the salt is derived from ammonia, ethylenediamine, N-methylglucamine, lysine, arginine or ornithine, when prepared by the process defined in Claim 1 or by an obvious chemical equivalent.

14. A compound selected from:



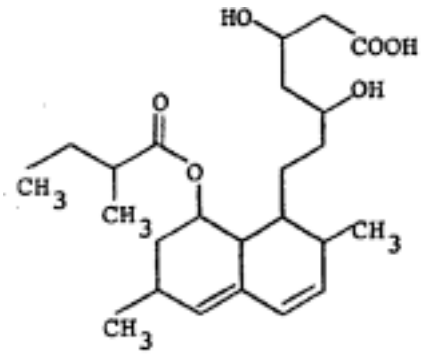
I



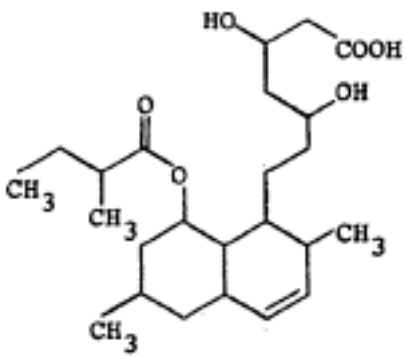
II

when prepared by the process defined in Claim 2 or by an obvious chemical equivalent.

15. A compound selected from:



III



IV

when prepared by the process defined in Claim 5 or by an obvious chemical equivalent.

FEDERAL COURT
SOLICITORS OF RECORD

DOCKET:	T-1272-97
STYLE OF CAUSE:	Merck & Co Inc. and Merck Frosst Canada Ltd. v. Apotex Inc. and Apotex Fermentation Inc. Biogal Pharmaceutical Works Ltd. (Third Party)
PLACE OF HEARING:	Toronto, Ontario
DATE OF HEARING:	February 1, 2, 3, 4, 2010; February 8, 9, 10, 11, 2010 February 16, 17, 18, 19, 2010; February 22, 24, 2010 March 1, 2, 3, 4, 5, 2010; March 8, 10, 11, 2010 March 16, 17, 18, 19, 2010; March 22, 23, 24, 25, 2010 March 29, 30, 31, 2010; April 1, 15, 2010 May 17, 18, 19, 20 and 21, 2010
PUBLIC REASONS FOR JUDGMENT:	SNIDER J.
DATED:	December 22, 2010

APPEARANCES:

Andrew J. Reddon Glynnis P. Burt David Tait William H. Richardson Ariel Neuer	FOR THE PLAINTIFFS
Harry Radomski Jerry Topolski Ben Hackett David Scrimger	FOR THE DEFENDANT APOTEX INC.
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