

Federal Court



Cour fédérale

**Date: 20100630**

**Docket: T-371-08**

**Citation: 2010 FC 714**

**BETWEEN:**

**ASTRAENECA CANADA INC.  
AND ASTRAZENECA AKTIEBOLAG**

**Applicants**

**- and -**

**APOTEX INC. AND THE MINISTER OF HEALTH**

**Respondents**

**REASONS FOR JUDGMENT**

**HUGHES J.**

[1] This is an application brought by AstraZeneca Canada Inc. and AstraZeneca Aktiebolag (collectively AstraZeneca) under the provisions of the *Patented Medicines (Notice of Compliance) Regulations*, SOR/93 – 133, as amended (*NOC Regulations*), for an Order prohibiting the Respondent, Minister of Health, from issuing a Notice of Compliance to the other Respondent, Apotex Inc., for 20 and 40 mg esomeprazole magnesium tablets until after the expiry of Canadian Patent No. 2,139,653 (the ‘653 patent). For the reasons that follow, I will dismiss the application with costs to Apotex at the column 4 level.

## THE PARTIES

[2] The Applicants, described as the “first person” in the *NOC Regulations*, are AstraZeneca Canada Inc., the Canadian licensee and AstraZeneca Aktiebolag the owner, respectively, of the ‘653 patent. They are also sometimes described as “the brand” or “innovators”. The Respondent Apotex Inc. described as a “second person” in the *NOC Regulations*, is a Canadian generic drug company who wishes to sell a generic version of AstraZeneca’s esomeprazole product in Canada. The Minister of Health is responsible for administering the *NOC Regulations* and is required to issue a Notice of Compliance to Apotex to sell its generic drug in Canada if this application is dismissed.

## THE DRUG AND INSTITUTION OF THESE PROCEEDINGS

[3] AstraZeneca has received a Notice of Compliance to sell a drug in Canada containing esomeprazole magnesium as an active ingredient. This drug is sold under the brand name NEXIUM in 20 and 40 mg strength tablets. It is said to be useful in the treatment of conditions wherein a reduction of gastric acid secretion is required, such as reflux esophagitis, nonerosive reflux disease and NSAID-associated gastric ulcers.

[4] Apotex wishes to sell a generic version of this drug in Canada and has applied through the Abbreviated New Drug Submission (ANDS) procedure under the *Food and Drug Act*, R.S.C. 1985, c. F-27 to receive a Notice of Compliance permitting it to do so. In that regard, Apotex as was required by the *NOC Regulations* served a Notice of Allegation, dated January 17, 2008, on AstraZeneca alleging that the ‘653 patent which AstraZeneca had listed under the *NOC Regulations*, was invalid, and would not be infringed. Whereupon AstraZeneca commenced these proceedings

pursuant to the *NOC Regulations* to prohibit the Minister from granting a Notice of Compliance to Apotex until the expiry of the '653 patent. The issues have been reduced so that what remains for determination is only whether Apotex's allegations that claim 8 of the '653 patent is invalid on a number of grounds, are justified within the meaning of section 6(2) of the *NOC Regulations*.

[5] By an Order of a Prothonotary of this Court, granted on consent on August 26, 2009, the 24-month statutory stay pursuant to section 7 of the *NOC Regulations* was extended to September 30, 2010.

#### HISTORY OF OMEPRAZOLE LITIGATION IN CANADA

[6] AstraZeneca has been zealous in enforcing patents that it has secured in Canada relating to omeprazole based products, of which the current application is one.

[7] Apotex has been equally zealous in seeking approval for generic versions of the drug:

In *AstraZeneca Canada Inc. v. Canada (Minister of Health)*, [2006] 2 S.C.R. 560, 2006 SCC 49, the Supreme Court of Canada allowed an appeal from the Court of Appeals which quashed Apotex's NOC. The Supreme Court held that the Federal Court was correct that Apotex was not required to address the after-issued patents of AstraZeneca. Here, the Court dealt with a situation where AstraZeneca's original patent directed to omeprazole had expired, it discontinued its original formulation and had commenced to market a new formulation. Applicants listed under the *NOC Regulations*, two patents directed to the new

formulation. Apotex wanted to market the original formulation and a question arose whether it could do so.

<http://scc.lexum.umontreal.ca/en/2006/2006scc49/2006scc49.html>

In *AB Hassle v. Apotex Inc.*, 2002 FCT 931, AstraZeneca assumed a patent directed to the coating of omeprazole cores with a subcoat or a coat to provide for enteric release. Apotex was precluded from getting an NOC to sell the product because its Notice of Allegations did not comply with the *NOC Regulations*. The Court found the NOA deficient in that it lacked detailed statements of the legal and factual basis for the allegation of non-infringement.

<http://decisions.fct-cf.gc.ca/en/2002/2002fct931/2002fct931.html>

In *AB Hassle v. Canada (Minister of National Health and Welfare) (T.D.)*, [2002] 3 F.C. 221, 2001 FCT 1264, Apotex was granted the NOC because the Court held that the patent would not be infringed. AstraZeneca filed the patent for the use of omeprazole in the treatment of *Campylobacter* infections. Apotex sought to market omeprazole for another use which would not be for the treatment of *Campylobacter* infections.

<http://decisions.fct-cf.gc.ca/en/2001/2001fct1264/2001fct1264.html>

In *AstraZeneca AB v. Apotex Inc.*, 2004 FC 313, the Court dismissed the application and allowed the Minister to issue the NOC to Apotex. The Court held that the patent in issue would not be infringed. Apotex sought approval for its drug containing only omeprazole to be used to treat conditions where the reduction of gastric acid secretions is required.

Applicants' patent covered a combination product containing omeprazole and an antibiotic.

<http://decisions.fct-cf.gc.ca/en/2004/2004fc313/2004fc313.html>

In *AB Hassle v. Apotex Inc.*, 2003 FCT 771, the Court prohibited the Minister from issuing an NOC to Apotex when the Court held that adding base salts to omeprazole was a novel invention not known or disclosed in prior art.

<http://decisions.fct-cf.gc.ca/en/2003/2003fct771/2003fct771.html>

*AstraZeneca AB v. Apotex Inc.*, 2005 FCA 183, is an appeal by AstraZeneca from the trial court's decision to dismiss its application and grant the NOC to Apotex. The Court of Appeal held that Apotex's NOA was sufficient in its allegations and there were no reversible errors. Apotex had previously submitted and withdrew an NOA which alleged its product would have 70% crystallinity of an amorphous form of omeprazole which would thereby infringe Applicants' product. The trial court held that since the newer NOA was separate and distinct and Apotex's product would not infringe the innovator's product.

<http://decisions.fca-caf.gc.ca/en/2005/2005fca183/2005fca183.html>

*AB Hassle v. Apotex Inc.*, 2004 FC 379, is an application under the *NOC Regulations* where two patents claim new uses for omeprazole or its salts to be used in combination with an antibiotic to act as an antimicrobial agent. The application for prohibition was dismissed because Apotex's product would only comprise omeprazole as its sole active ingredient for use in the reduction of gastric acid secretion.

<http://decisions.fct-cf.gc.ca/en/2004/2004fc379/2004fc379.html>

*AstraZeneca AB v. Apotex Inc.*, 2006 FC 7, appeal dismissed, the application was dismissed because the Court held that the enteric coating of Apotex's product made the formulation different and therefore would not infringe AstraZeneca's product.

<http://decisions.fct-cf.gc.ca/en/2006/2006fc7/2006fc7.html>

In *AB Hassle v. Apotex Inc.*, 2005 FC 234, the Court granted the prohibition under the doctrine of *issue estoppel* in that Apotex could have brought its current allegations in a previous proceeding.

<http://decisions.fct-cf.gc.ca/en/2005/2005fc234/2005fc234.html>

In *AstraZeneca AB v. Apotex Inc.*, 2007 FC 688, the application was dismissed when the Court held the allegations of invalidity were justified in that prior art anticipated the claims in issue and some of the claims did not contain any therapeutic aspects.

<http://decisions.fct-cf.gc.ca/en/2007/2007fc688/2007fc688.html>

[8] Other generic companies have not been as successful as Apotex. So far, none have been granted an NOC:

In *Genpharm Inc. v. AB Hassle*, 2004 FCA 413, the Court of Appeal affirmed the trial court's decision to grant the application for prohibition. Genpharm did not address non-infringement of all the claims in issue where some addressed taking omeprazole in combination with an antibiotic. Therefore, it did not advance the facts to support its allegation of non-infringement of those claims adequately enough.

<http://decisions.fca-caf.gc.ca/en/2004/2004fca413/2004fca413.html>

In *Hassle v. Canada (MNH)*, T-366-98, appeal affirmed, the Court granted the prohibition holding that the generic product of RhoxalPharma would include an inert subcoating thereby infringing AstraZeneca's product.

[http://decisions.fct-cf.gc.ca/en/2000/t-366-98\\_12522/t-366-98.html](http://decisions.fct-cf.gc.ca/en/2000/t-366-98_12522/t-366-98.html)

In *AB Hassle v. Rhoxalpharma Inc.*, 2002 FCT 780, the Court granted the prohibition because of a concern that doctors would prescribe the generic version of the pill for uses in the treatment of *H. pylori* infections and other bacterial infections even though RhoxalPharma's product monograph would specifically state its use is only for the reduction of gastric acid secretions.

<http://decisions.fct-cf.gc.ca/en/2002/2002fct780/2002fct780.html>

#### THE WITNESSES AND EVIDENCE

[9] This application, as is common in many NOC applications, began with raising a number of issues, and issues within those issues. AstraZeneca put a number of claims of the '653 patent at issue, including claims 3, 7, 8, 27 and 28. Apotex was arguing non-infringement of several of those claims, as well as certain "bad faith" arguments arising out of section 53 of the *Patent Act, R.S.C. 1985, c.P-4*. As a result, there was some evidence filed which subsequently has become irrelevant. As well, the evidence of several witnesses became relevant only in respect of certain matters. I list all the witnesses, both expert and factual, whose evidence was filed by each party.

**1. Applicants' Witnesses – ASTRAZENECA**

[10] Applicants filed affidavit evidence from the following Expert Witnesses: Dr. Armstrong, Dr. Davies, and Dr. Nelson. Affidavits from the following fact witnesses were filed: Dr. Larsson, Dr. Andersson, Ms. Feltmate, Dr. Kohl, Dr. Senn-Bilfinger, Dr. von Unge, and Ms. De Abreu.

**a. Dr. Daniel Armstrong – EXPERT**

Dr. Armstrong is the Robert A. Welch Professor, in the Department of Chemistry and Biochemistry at University of Texas at Arlington. He received a B.Sc. in interdepartmental science and math in 1972 from Washington & Lee University, Lexington, Virginia. In 1974, he obtained a Master's of Science in oceanography from Texas A&M University, College Station, Texas. In 1977, he received a Ph.D. in bio-organic chemistry, from Texas A&M University. The focus of his research has been on methods for separating chiral compounds. He has published over 400 peer-reviewed articles in the academic literature and is a lecturer. He is named as inventor or co-inventor in 11 patents.

**i. Mandate**

Dr. Armstrong was asked: to describe the person of ordinary skill in the art (“POSITA”) to whom the Canadian Patent 2,139,653 (“’653 patent”) is addressed; and to rebut Apotex’s allegations of lack of novelty, lack of invention and willful misleading when looking at the ‘653 patent.

**b. Dr. Stephen Davies – EXPERT**

Dr. Davies is the Chairman of the chemistry department at the University of Oxford, where he has been teaching since 1980. He is also currently the Waynflete Professor of Chemistry at the University of Oxford. He earned a B.A. degree in 1973 and a D. Phil. Degree in 1975, both in Chemistry from the University of Oxford. He obtained a D.Sc. degree in Chemistry from the University of Paris in 1980. His research focuses on the preparation of enantiomerically pure compounds. Dr. Davies founded a company, Oxford Asymmetry, Ltd. In 1992 that provides homochiral compounds in commercial quantities.

**i. Mandate**

Dr. Davies was asked: to describe POSITA to whom the Canadian '653 patent is addressed; to explain the '653 patent, in particular claims 7 and 8, from the view of the POSITA on December 8, 1994; and to rebut Apotex's allegations of invalidity of the '653 patent, particularly anticipation, lack of invention – obviousness and Section 53 – wilful misleading.

**c. Dr. Wendel Nelson – EXPERT**

Dr. Nelson is a professor in the Department of Medicinal Chemistry, University of Washington, Seattle, Washington. He received a B.S. in Pharmacy from Idaho State College in 1962 and a Ph.D. in Pharmaceutical Chemistry from the University of Kansas in 1965. Since 1965, he has been a Professor at the University of Washington. He considers himself an expert in the area of medicinal chemistry and researches the chemical and stereochemical aspects of the metabolism of cardiovascular drugs.

**i. Mandate**

Dr. Nelson was asked: to describe POSITA to whom the Canadian '653 patent is addressed; to explain the '653 patent, in particular claims 7 and 8, from the view of the POSITA on December 8, 1994; and to rebut Apotex's allegations of invalidity of the '653 patent, particularly obviousness and lack of sound prediction.

**d. Dr. E. Magnus Larsson – FACT**

Dr. Larsson is currently employed as the Director of the Process Chemistry Group for AstraZeneca AB in Sweden. He was directly involved with research and development of manufacturing processes for the esomeprazole magnesium trihydrate. He is named as an inventor in about 58 patents related to his research. In 1985, he earned an M.S. in chemical engineering at the Royal Institute of Technology in Stockholm. Dr. Larsson received his Ph.D. degree in 1993 in organic chemistry from the Royal Institute of Technology.

**i. Mandate**

Dr. Larsson was asked to discuss the work he did at AstraZeneca in 1993 with respect to making omeprazole enantiomers using the process identified in the DE 4035455 patent ("DE 455 patent").

**e. Dr. Tommy Andersson – FACT**

Dr. Andersson received a B.Sc. in Biology and a Ph.D. in Clinical Pharmacology in 1979 and 1991, respectively, from the University of Gothenburg, Sweden. In 1979, he joined Hassle AB, now AstraZeneca AB, and worked in the pre-clinical research group

in the Pharmacology Department. In 1981, he moved to the clinical pharmacology group where he became involved with omeprazole. In 1993, he was appointed Project Team Leader for the Omeprazole Successor Project at AstraZeneca AB.

**i. Mandate**

Dr. Andersson was asked: to describe the testing of esomeprazole alkaline salts in the context of the Omeprazole Successor Project at AstraZeneca AB, to describe the metabolic and pharmacokinetic properties of esomeprazole; and the resulting tests and trials that demonstrate these properties and improved clinical effects of esomeprazole magnesium.

**f. Dr. Bernhard Kohl – FACT**

Dr. Kohl is currently employed as Senior Director Process Chemistry for Nycomed GmbH in Konstanz, Germany where he supervises 40 people. He earned an equivalent of a masters degree in organic chemistry in 1976 and a Ph.D. in organic chemistry in 1979, both at the University of Munich. Dr. Kohl is named as a co-inventor in the DE '455 patent application.

**i. Mandate**

Dr. Kohl's mandate is to discuss the developments in research in the proton pump inhibitor field and the developmental history of the DE '455 patent application.

**g. Dr. Johann Senn-Bilfinger – FACT**

Dr. Senn-Bilfinger is currently employed as a Director of Discovery and Proof of Concept Development by Nycomed GmbH in Konstanz, Germany. He has been employed by Nycomed, its predecessor Altana Pharma AG and its predecessor Byk Gulden Lomberg Chemische Fabrik GmbH, since 1978. He earned a Diploma degree in chemistry in 1975 from the University of Stuttgart, Germany and completed a doctorate in chemistry at the University of Stuttgart, in 1978. Dr. Senn-Bilfinger is named as a co-inventor in the DE '455 patent application.

**i. Mandate**

Dr. Senn-Bilfinger's mandate is to discuss the developments in research in the proton pump inhibitor field and the developmental history of the DE '455 patent application.

**h. Dr. Sverker Von Unge – FACT**

Dr. Von Unge is a principal scientist in the Medicinal Chemistry department at AstraZeneca R&D (formerly Hassle AS) and has been employed there since 1988. He obtained a Master of Science in Engineering in 1983 from Chalmers University of Technology in Sweden. He is named as a co-inventor of the '653 patent.

**i. Mandate**

Dr. Von Unge's mandate was to discuss his involvement in the developmental history of the '653 patent.

**i. Ms. Karen Feltmate – FACT**

Ms. Feltmate is the Vice-President of Operations, Business Services and Regulatory Affairs at AstraZeneca Canada Inc.

**i. Mandate**

Ms. Feltmate provided a copy of Apotex's Notice of Allegation.

**j. Ms. Jacinta De Abreu – FACT**

Ms. De Abreu is a law clerk at Smart & Biggar.

**i. Mandate**

Ms. De Abreu provides certain documents as exhibits.

**2. Respondent's Witnesses – APOTEX**

[11] Respondent filed the affidavit evidence of the following Expert Witnesses: Dr. Heathcock, Dr. Collicott, Dr. Caldwell, Dr. Mayersohn and Dr. Myerson. Affidavits from the following fact witnesses were filed: Dr. Batey, Dr. Bihovsky and Ms. Ebdon.

**a. Dr. Clayton Heathcock – EXPERT**

Dr. Heathcock is currently the Emeritus Professor at the University of California at Berkeley and Chief Scientist of the Berkeley branch of the California Institute for Quantitative Biosciences. He obtained a Bachelor of Science from Abilene Christian College, Texas, in 1958 and a Ph.D. in Organic Chemistry from the University of Colorado in 1963. His research focuses on the development of new synthetic and natural products in chemistry.

**i. Mandate**

Dr. Heathcock was asked: to describe POSITA to whom the Canadian '653 patent is addressed; to comment on the '653; to give a background on racemates and separation techniques; and to comment on various affidavits of Applicants' witnesses.

**b. Dr. Roland Collicott – EXPERT**

Dr. Collicott is the owner of ChalPharm Consultancy, which provides consulting services to the pharmaceutical industry in the area of analytical chemistry, including training courses for analytical chemists, drug characterization, chiral and polymorphic analysis, stability studies, etc. He is an analytical chemist and has worked at Glaxo Group Research Ltd., OSI Pharmaceuticals (UK) Ltd. as well as other companies. He received his Ph.D. in 2002 from Open University.

**i. Mandate**

Dr. Collicot was asked: to describe POSITA to whom the Canadian '653 patent is addressed; to comment on the '653; to give a background on chromatography and the separation of enantiomers; and to comment on various affidavits of Applicants' witnesses.

**c. Dr. John Caldwell – EXPERT**

Dr. Caldwell is the Dean of the Faculty of Medicine of the University of Liverpool, England, since 2002. He was also appointed a Pro-Vice Chancellor of the University in 2007. He received a Bachelor of Pharmacy in 1969 from the University of London and a

Ph.D. in biochemistry in 1972. In 1987, the University of London awarded him the degree of Doctor of Science (DSc) in pharmacology, for distinctions in drug metabolism.

**i. Mandate**

Dr. Caldwell was asked: to provide a technical primer on issues of stereochemistry, pharmaceuticals, pharmacokinetics and metabolism as would be known by the POSITA as of December 1994 and as of May 1993; to comment on the '653; and to comment on Apotex's allegations of invalidity of the '653 patent, particularly lack of invention.

**d. Dr. Michael Mayersohn – EXPERT**

Dr. Mayersohn is a Professor of Pharmaceutical Sciences, College of Pharmacy, University of Arizona. He received a Bachelor of Science in Pharmacy from Columbia University in 1966 and obtained a Ph.D. in pharmaceuticals from the State University of New York at Buffalo in 1971.

**i. Mandate**

Dr. Mayersohn was asked: to describe the POSITA to whom the Canadian '653 patent is addressed; to comment on the '653 patent; and to comment on Apotex's allegations of invalidity of the '653 patent, particularly lack of utility and lack of sound prediction.

**e. Dr. Allan Myerson – EXPERT**

Dr. Myerson is currently the Philip Danforth Armour Professor of Engineering, in the Department of Chemical and Biological Engineering at the Illinois Institute of Technology in Chicago. He obtained a Bachelor of Science in chemical engineering in May 1973 and Masters and Ph.D. degrees in chemical engineering from the University of Virginia in January 1975 and January 1977, respectively. He is a registered Professional Engineer in New York and Ohio. His research focuses on crystallization from solution.

**i. Mandate**

Dr. Myerson was asked: to give a background on crystals and crystallization as the POSITA who have known on May, 28, 1993 and December 8, 1994; to describe the POSITA to whom the Canadian '653 patent is addressed; to comment on the '653 patent; and to comment on the prior art as it pertains to statements made in the affidavits of Applicants' witnesses.

**f. Dr. Robert Batey – FACT**

Dr. Batey is currently a Professor of Chemistry and the Associate Chair of Undergraduate Studies at the University of Toronto. In 1992, he received a Ph. D. in chemistry from the Imperial College of Science, Technology and Medicine in London.

**i. Mandate**

Dr. Batey performed an analysis using HPLC on two samples of solid material provided by Respondent in order to determine the enantiomeric excess of each sample.

**g. Dr. Ron Bihovsky – FACT**

Dr. Bihovsky is an organic chemist. In 2001, he founded Key Synthesis LLC, a chemistry laboratory that performs contract research for pharmaceutical and biotechnology companies, process research, and consulting work in synthetic organic chemistry and medicinal chemistry. He obtained a Ph.D. in chemistry at the University of California Berkeley in 1977.

**i. Mandate**

Dr. Bihovsky was asked to repeat Examples 5 and 6 in the DE 455 patent as a POSITA would have done on May 28, 1993.

**h. Ms. Lisa Ebdon – FACT**

Ms. Ebdon is a law clerk employed by Goodmans LLP.

**i. Mandate**

Ms. Ebdon produced many of Apotex's documentary exhibits.

**3. Unreferred to Witnesses**

**a. ASTRAZENECA**

[12] Dr. Stephen Byrn submitted an expert affidavit that was not referred to in argument. He is a Professor of Medicinal Chemistry at Purdue University in Indiana. He received a Ph.D. in organic and physical chemistry in 1970 from the University of Illinois.

**i. Mandate**

Dr. Byrn was asked to comment on the Apotex's allegations of non-infringement of Canadian '653 patent. In particular, Apotex's assertions that Claim 3 of the '653 Patent will not be infringed because Apotex's product is not in a crystalline form.

**b. APOTEX**

[13] Shufeng Lui is an analytical chemist at Apotex whose mandate was to ship samples to Dr. Bihovsky.

[14] Ms. Michele Cossette is a second year student at the laboratory of Dr. Batey. She signed for the shipment and gave it to Dr. Batey's laboratory.

[15] Farhad Nowrouzi is a third year student at the laboratory of Dr. Batey. He signed for the shipment and gave the bottle received of racemic omeprazole to Dr. Batey.

[16] Dr. John Hems is the Director, Regulatory Affairs, Canada, for the Respondent, Apotex Inc. He provided an affidavit dealing with Apotex's ANDS submission history.

[17] Ms. Rosa Rahimpour is a scientist employed in the Toronto offices of Goodmans LLP. She was involved with tracking the shipments from Dr. Bihovsky.

#### **4. Uncontested Submissions**

[18] No party raised an objection as to the expert evidence of the other party as being properly tendered as expert evidence nor were the qualifications or expertise of such witnesses seriously questioned. I accept, therefore, such evidence as expert evidence.

[19] The parties jointly tendered a book containing the following documents as agreed documents. These documents appear in the Record; therefore, the book was not separately marked as an exhibit. However, it is noted that these documents were accepted as proper evidence without further proof being required:

1. Copy of Apotex's Notice of Allegation (pages 845 to 915 of the Record);
2. Copy of the '653 patent (pages 388 to 416 of the Record);
3. Copy of an agreed-upon English language translation of German Patent Application DE 40 35 455 (the DE '455 application) available for public inspection May 14, 1992. A copy of the original document in the German language was also provided. The German language document appears in the Record at pages 250 to 257; the English translation from which the parties and the Court worked is at pages 258 to 276 of the Record;

4. Copy of a scientific article by Erlandsson et al entitled “Resolution of enantiomers of esomeprazole...” appearing in Journal of Chromatography, published in 1990, section 532, no. 2, November 16, 1990, pages 305 – 313 (the Erlandsson article) as appears in the Record at pages 1386 to 1402.

[20] No witnesses appeared before me in person. Transcripts of their cross-examinations were provided. I have no basis for finding that any witness should be considered to lack credibility. Some arguments were raised as to hearsay, which I will deal with below.

#### HEARSAY

[21] Apotex objects to certain testimony contained in the affidavits of some of the AstraZeneca witnesses as being inadmissible on the basis that it is hearsay. In particular, Apotex objects to the following:

- Paragraph 37 of the Senn-Bilfinger affidavit, page 216 of the Record;
- Paragraphs 58 to 63, 65 and 67 of the Kohl affidavit, pages 145 and 146 of the Record; and
- Paragraphs 32 to 36 of the Larsson affidavit, pages 230 and 231 of the Record.

[22] Each of the above passages are objected to by Apotex on the basis that the witness is attesting that certain scientific work was carried out and certain results were achieved or not achieved however, that work was not done by the person swearing the affidavit, but by someone else.

[23] AstraZeneca replies by saying that the work was supervised by and done in conjunction with the person swearing the affidavit, and done in the normal course of the duties of the affiant and the persons carrying out those tasks. AstraZeneca points to evidence tendered by Apotex's witness Dr. Bihovsky, where certain tests were conducted by others and accepted by Dr. Bihovsky. AstraZeneca does not object to that evidence.

[24] I have read the portions of the affidavits objected to and the portions of the transcripts of the cross-examination of those witnesses. I have no hesitation in ruling inadmissible paragraph 37 of the Senn-Bilfinger affidavit in which he speaks about certain results recorded in Dr. Kohl's notebook, as it is clear from the answers he gave during his cross-examination at pages 14 to 16, 40 to 46 and 54 to 57, that he knew nothing of the Kohl notebook in question or what is recorded there.

[25] As to the other evidence to which objection is taken, the relevant portions of the transcripts of the cross-examination (Kohl: pages 13, 14, 24, 25, 64 to 66, 71 to 77, 81, 82, 96 to 99) (Larsson: pages 43 to 45, and portions of Niman's notebook) satisfy me that AstraZeneca's representation of the facts is correct, those affiants did supervise the work done by others in the normal course of the duties of each of them.

[26] Apotex relies on Rule 81 of this Court to state that affidavit evidence shall be confined to facts within the personal knowledge of the deponent. It also relies on the decision of the Federal Court of Appeal in *Canadian Tire Corporation Limited v. P.S. Partsource Inc.*, 2001 FCA 8 in arguing that while a Court may relieve a party from the obligations of Rule 81, it must do so by way of a motion brought before the hearing with a showing that the evidence is reliable and necessary. The decision

of Mosely J. of this Court in *Pfizer Canada Inc. v. Apotex Inc.* (2007), 61 C.P.R. (4<sup>th</sup>) 305, at paragraphs 112 to 115 is to the same effect.

[27] I am guided by *Sopinka, Lederman & Bryant "The Law of Evidence in Canada"*, 3<sup>rd</sup> ed., LexisNexis in dealing with Apotex's objection. At pages 269 and 270 of *Sopinka*, there is a discussion respecting the flexible approach that a Court must take in looking at objections of this sort. The Court should not be pigeon-holed by a set of rules respecting reliability and necessity. Flexibility does not mean that admissibility is limitless, but the Court must be guided by the circumstances of each case. At pages 283 to 291 of *Sopinka*, there is a discussion as to the common law rule respecting admissibility of business records. There is such a rule to the effect that business records made in the ordinary course contemporaneously with the events, without motive or interest to misstate the facts, are admissible. To some extent, this rule was at one time hampered by a requirement that the person making the record be deceased, but this appears no longer to be the case. To a large extent the matter may be overshadowed by statutes respecting admissibility of business records; but those statutes do not eliminate the common law rule. The common law rule remains such that a Court, in the circumstances of each case before it, on a flexible basis, may admit evidence of the kind at issue here.

[28] Having reviewed the remaining evidence, I find that it relates to work done in the ordinary course of the duties of the persons recording it, the records were made contemporaneously, and I find no reason to believe that there was falsification or any motive or interest to falsify what was recorded. I hold that the evidence at issue, except as to Senn-Bilfinger, as aforesaid, is admissible.

### THE '653 PATENT

[29] At issue is Canadian Letters Paten No. 2,139,653 (the '653 patent). That patent, entitled “*Optically Pure Salts of Pyridinylmethyl Sulfinyl – IH – Benzimidazole Compounds*” was issued and granted to AstraZeneca Aktiebolag on July 10, 2007. The application for that patent was filed in the Canadian Patent Office on May 27, 1994, thus the term of the patent, provided all maintenance fees are paid and the patent is not expunged, will expire twenty years from that date, May 27, 2014. The application claims priority from an application filed in Sweden on May 28, 1993. The application was laid open and available to the public (publication date) on December 8, 1994. Per Lindberg and Sverker von Unge, both of Sweden, are named as inventors.

[30] Since the application for the patent was filed with the Canadian Patent Office after October 1, 1989, the “new” provisions of the *Patent Act* apply to the application and the patent.

[31] The parties have agreed that the “claim date” relevant for the determination of some of the matters put in issue is the priority filing date - May 28, 1993.

### THE ISSUES

[32] The overriding issue is whether the allegations made by Apotex in its Notice of Allegation that claim 8 of the '653 patent is invalid, are justified within the meaning of section 6(2) of the *NOC*

*Regulations*. Some of the allegations made in that respect have been dropped by Apotex. The following allegations remain in contention:

1. Lack of Sound Prediction as to utility;
2. Anticipation having regard to the state of the art and the German application DE ‘455; and
3. Obviousness having regard to the state of the art, DE ‘455 and the Erlandsson article

[33] In order to address these matters, the Court must first address the following:

- a) Who is the person skilled in the art to whom the patent is addressed?
- b) What was the state of the art at the relevant time?
- c) What was the problem that the patent addresses?
- d) What is the solution offered to that problem by the patent?
- e) What is the proper construction of claim 8?
- f) Who bears the burden of proof?

a) **Who is the person skilled in the art to whom the patent is addressed?**

[34] The ‘653 patent begins with a statement as to the Field of the Invention:

*Field of the Invention*

*The present invention is directed to new compounds with high optical purity, their use in medicine, a process for their preparation and their use in the manufacture of pharmaceutical preparation. The invention also relates to novel intermediates in the preparation of the compounds of the invention.*

[35] In the Background discussion that follows, it is stated that the patent deals with omeprazole; and more particularly, one of its enantiomers, esomeprazole, all of which is part of the prior art. The patent thereafter states that it deals particularly with an improved process for making very pure esomeprazole, and very pure esomeprazole itself.

[36] Each of the parties provided, through a number of expert witnesses, opinions as to a proper characterization of the person to whom the patent is addressed - the person of ordinary skill in the art (POSITA). For Apotex, representative of what its experts say is Dr. Myerson at paragraph 35:

*35. Based on the subject matter of the 653 Patent, in my opinion the person of ordinary skill in the art to whom the patent is addressed would include organic and medicinal chemists. Such persons would have a Bachelors, Masters or Ph.D. degree in chemistry, chemical engineering or related fields, with at least a few years of experience in either academics or the chemical or pharmaceutical industry. Such a person would also have a working knowledge of the principles of stereochemistry, analytical techniques for separating enantiomers, salt formation and properties, and crystals and crystallization. The person of ordinary skill in the art would also include pharmacologists with experience in pharmacokinetics and metabolism.*

[37] For AstraZeneca, representative of what its experts say is Dr. Armstrong, at paragraph 103:

*E. Person of Ordinary Skill in the Art*

*103. I have been asked to comment on the education and experience of a skilled person to whom the '653 patent is addressed. Based on my reading of the '653 patent, the skilled person to whom this patent is addressed would include a person or persons having an M.S. or a B.X. degree in organic, analytical, medicinal or pharmaceutical chemistry, plus 3 to 5 years work experience in techniques relating to separation and purification of organic/pharmaceutical molecules, or having a Ph.D. degree in organic, analytical, medicinal or pharmaceutical chemistry having*

*experience in separation and purification of organic/pharmaceutical molecules.*

[38] In cross-examination, particularly in answer to questions 337 to 341 (pages 6317 – 6318 of the Record) Dr. Andersson agreed that such a person would also be involved in pharmacokinetics and pharmacology. Therefore, his view of a person of ordinary skill in the art essentially coincides with that of Dr. Myerson, whose definition I accept and adopt as appropriate for a POSITA respecting the '653 patent.

[39] I repeat what I wrote in *Merck & Co. Inc. v. Pharmascience Inc.*, May 11, 2010, 2010 FC 510 at paragraphs 38 and 40, respecting a POSITA:

*38 In dealing with individual cases, the Court must guard against making too fine a distinction as to identifying the "ideal" POSITA. Counsel for each party will argue meanings and shades of meanings most favourable to their case and the witness(es) they present. Each Counsel will argue that their witness(es) best fit the description of the ideal POSITA while there are numerous shortcomings with each of the witness(es) for the opposing party.*

...

*40 To require fine precision and ranking of voices is to place a series of "trip wires" upon which a Court may be expected to stumble or risk sanctions by a higher Court. There must be some generalized treatment of the question of defining a POSITA and a level of generalization applied.*

b) **What was the state of the art at the relevant time?**

[40] In this regard, one may start with what the '653 patent says that the state of the art was.

Statements made in a patent as to the state of the art are binding on the patentee (*Whirlpool Corp. v. Camco Inc.* (1997), 76 C.P.R. (3<sup>rd</sup>) 150 at page 186 (F.C.) aff'd (1999), 85 C.P.R. (3<sup>rd</sup>) 129 (F.C.A.)

and [2000] 2 S.C.R. 1067; *Shire Biochem Inc. v. Canada (Minister of Health)* (2008), 67 C.P.R. (4<sup>th</sup> 94 at para. 24 (F.C.A.).

[41] At page 1, following the title “Background of the Invention”, the ‘653 patent acknowledges that the following is part of the state of the art preceding the making of the alleged invention:

- Omeprazole and its salts is a known compound:  
*The compound 5-methoxy-2-[[[4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole, having the generic name omeprazole, and therapeutically acceptable alkaline salts thereof are described in EP 5129 and EP 124 495, respectively.*
- Omeprazole has a known use; it is effective in dealing with gastric acids and ulcers:  
*Omeprazole and its alkaline salts are effective gastric acid secretion inhibitors, and are useful as antiulcer agents*
- Omeprazole can exist as two optical isomers (enantiomers):  
*The compounds, being sulfoxides, have an asymmetric center in the sulfur atom, i.e. exist as two optical isomers (enantiomers)*
- The Erlandsson article previously referred to describes the resolution of the enantiomers of omeprazole on an analytical scale, and DE ‘455 previously referred to describes the same in a preparative scale. (These are the two pieces of prior art principally relied upon by Apotex):  
*The separation of the enantiomers of omeprazole in analytical scale is described in e.g. J. Chromatography, 532 (1990), 305-19(Erlandsson) and in a preparative scale in DE 4035455.*
- DE ‘455 has disadvantages, being devastating localized pH values and heat generation, which is difficult to handle in large scale production:

*The latter has been done by using a diastereomeric ether which is separated and thereafter hydrolysed in an acidic solution. Under the acidic conditions needed for hydrolysis of the attached group, omeprazole is quite sensitive and the acid has to be quickly neutralized with a base to avoid degradation of the acid-sensitive compound. In the above mentioned application this is done by adding the reaction mixture containing concentrated sulphuric acid to a concentrated solution of NaOH. This is disadvantageous because there is a great risk of locally reaching pH values between 1-6 which would be devastating for the substance. Moreover, instantaneous neutralisation will create heat which will be difficult to handle in large scale production.*

[42] During the course of argument at the hearing of this matter, AstraZeneca's counsel made reference to paragraph 16 of the affidavit of Dr. Mayersohn, one of Apotex's experts (page 5798 of the Record). In response to my question, counsel said that he agreed with the summary presented there:

*16. The '653 patent describes particular base addition salts of the enantiomers of omeprazole, their preparation, and their use as proton pump inhibitors of the generation of stomach acid. The '653 patent also cites references for the separation of the enantiomers on both analytical and preparative scales. Skilled persons reading the '653 patent already were aware that omeprazole and its two individual enantiomers were proton pump inhibitors.*

[43] AstraZeneca, in argument, put forward a portion of Dr. Caldwell's affidavit, an Apotex expert, and agreed with that portion as far as it went. I refer to paragraphs 114 and 115 (Record, page 5616), noting that the acronym PPI stands for "proton pump inhibitor", the proton pump being that which is found in the stomach that produces acid:

*114. Omeprazole was a blockbuster PPI – By May 1993, it was commonknowledge that omeprazole was a very successful drug that was useful to treat conditions that required the inhibition of gastric acid secretion in humans. This fact was described in many sources available to skilled persons including Lindberg et. al., "Omeprazole: The first Proton Pump Inhibitor."*

115. *Skilled persons were motivated to resolve omeprazole to its enantiomers and study their respective properties – Omeprazole was a drug that was known to be racemic. It was also known that both of its enantiomers were active as PPIs. It was also known that the two enantiomers of omeprazole might be metabolized differently.*

[44] Some of AstraZeneca’s expert witnesses asserted that the separation of omeprazole into its enantiomers was not an easy task; however, several known attempts, such as the Erlandsson article and DE ‘455 had been published. Dr. Armstrong said at paragraph 93 of his affidavit (Record, page 581):

93. *I have described some of the techniques available for separation and isolation of enantiomers. However, there are many different methods available, each of which has a number of different parameters and conditions that can be varied. Before attempting separation of a particular enantiomeric mixture, a skilled person would not know that the enantiomers could be separated and which methods, conditions and parameters to choose in order to be successful. Thus, the skilled person would be faced with a large number of possible approaches.*

[45] In cross-examination, Dr. Caldwell, one of Apotex’s experts, was directed to something he had previously written, and agreed that separation of enantiomers may be difficult, but it was not a reason not to try. He said in answer to questions 741 to 743 (Record, pages 781 – 782):

741

Q. *You write:*

*“Applicants must recognize the occurrence of chirality in new drugs, attempt to separate the stereoisomers, assess the contribution of the various stereoisomers to the activity of interest and then made a rational selection of the stereoisometric form that is proposed for marketing.”*

A. *Yes*

742                                    *Q.*     *To the extent that you say “attempt to separate the isomers” that contemplates that one cannot necessarily separate:*

*A.*     *Yes, it does –*

743                                    *Q.*     *Then over the page –*

*A.*     *-- but simply looking at it and saying: Oh, it's very difficult... is not a reason. Attempt is what's required.*

[46] Thus, the background to what the '653 patent describes as its invention can be summarized as follows:

- Omeprazole, including its salts, was a well known “blockbuster” drug useful in the treatment of gastric acid related conditions.
- It was known that omeprazole was racemic and comprised two enantiomers.
- At least two known successful attempts at separating omeprazole into its enantiomers had been published - the Elandsson article and DE '455.
- Both enantiomers were useful in treating gastric acid conditions.
- The separation of omeprazole into its enantiomers was not an easy task.

c)     **What was the problem that the patent addresses?**

[47] The '653 patent sets out the problem that it seeks to address at page 1 in the background section as follows:

*It is desirable to obtain compounds with improved pharmacokinetic and metabolic properties which will give an improved therapeutic profile such as a lower degree of interindividual variation. The present invention provides such compounds, which are novel salts of single enantiomers of omeprazole.*

[48] The patent, as previously noted, discusses the processes described in the Erlandsson article and DE '455. It does not say anything about the Erlandsson article other than that it describes an “analytical” scale process. The patent says that the DE '455 process is subject to localized pH issues and heat problems which make large-scale production difficult.

[49] The reference to “interindividual variation” is a phenomenon addressed by one of the inventors, Sverker von Unge, in his affidavit. He said at paragraph 6 (Record, page 1075):

*6. Despite the considerable success of omeprazole, it had some shortcomings, in particular interpatient variability, meaning that the drug (and other first-generation proton pump inhibitors (PPI's)) failed to suppress and/or sustain inhibition of acid production in some patients, and certain drug-drug interactions. These failings motivated Hassle to seek a new PPI with improved efficacy by producing greater acid suppression in a greater number of patients.*

[50] This interpatient variability exhibited by omeprazole was a known phenomenon, as stated by Dr. Nelson at paragraph 97 of his affidavit (Record, page 1009):

*97. As discussed previously, omeprazole was known to exhibit variation between individuals in (1) its therapeutic effect and (2) AUC, as was reported by Andersson 1990 (Apotex document 11), Regardh (Apotex document 10) and Sohn (Apotex document 32). First omeprazole had shown a significant degree of variation in treatment effect, or pharmacodynamic responsiveness based on measurements of gastric acid secretion. Second, PMs showed much greater AUC of omeprazole as compared to Ems, the rest of the population. It was known that about 3% of the Caucasian population and 15-17% of Chinese were PMs (summarized in Andersson 1992 (Apotex document 29)).*

[51] At the time, prior to 1993, it was believed that either enantiomer of omeprazole would act essentially the same way as omeprazole itself. Dr. Davies said at paragraphs 144 and 145 of his affidavit (Record, page 802):

*144. The mechanism suggests that the two enantiomers of omeprazole are inactive. The mechanism also suggests that the acid-mediated conversion of the two omeprazole enantiomers to the achiral sulfenamide occurs at the same rate. This was demonstrated experimentally by in vitro testing on the effects of omeprazole and its enantiomers on acid production in isolated rabbit gastric glands. (Erlandsson et al. at page 318).*

*145. In view of the mechanism of action of omeprazole, a skilled person would expect each enantiomer to have the same activity as the racemate. The skilled person would appreciate that the mechanism of action provides no incentive to obtain either enantiomer.*

[52] Similarly, Dr. Andersson said at paragraph 21 of his affidavit (Record, page 435):

*2. No pharmacodynamic advantage*

*21. It was believed, based on the mechanism of action of omeprazole, that omeprazole enantiomers would have the same pharmacological activity at the active site. As described above, inhibition at the active site is caused by the action of achiral sulfenamide. Upon entering the acidic environment of the canalfouli of the parietal cells, both enantiomers form the achiral sulfenamide at the same rate.*

[53] Also, as of 1993, there was some concern that, even if omeprazole was separated into its enantiomers, these enantiomers would not remain separated for long, and would tend to racemize; that is, recombine. Dr. Davies addressed this at paragraph 36 of his affidavit (as corrected) (Record, page 780):

*C. Racemization*

*36. Racemization is the conversion of a single enantiomer, through mixtures of the two enantiomers, to the racemic compound,*

*a 50:50 mixture termed the racemate. Sulfoxides [R(SO)R] are chiral when the two “R” groups are different as in [R(SO)R’], the sulphur becoming a stereogenic centre bearing four different attachments (R, R’, O and a pair of electrons). Racemization of sulfoxides commonly occurs by reversibly detaching and reattaching either of the R or R’ groups or by oxidation to the corresponding sulfone ([R(SO<sub>2</sub>)R’], in which the sulphur is no longer stereogenic, followed by reduction back to the sulfoxide. The skilled person would realize that omeprazole is particularly prone to the former racemisation process the nature of which facilitates the formation of the racemate. (Tab 4 in Schedule E Apotex’s Notice of Allegation).*

[54] Dr. Collicott, during his cross-examination in answer to questions 179 to 204 (Record, pages 7099 – 7105), which I will not repeat in full, agreed that as of 1993, racemisation was something that had to be borne in mind, but had not, as of that time, been extensively considered. I repeat questions and answers 200 to 203:

*MR. BRODKIN: That’s fair, and you’re asking as of May 1993?*

*BY MR. GAIKIS:*

200            *Q.      Correct.*  
                   *A.      I’m not sure how many examples there have been as of May 1993 of –*

201            *Q.      Examples of what?*  
                   *A.      Of racemisation, of column racemisation. I mean, it says it’s not been extensively considered. I mean, some people have looked at it, I know.*

202            *Q.      Extensively?*  
                   *A.      Some people have had individual compounds that have racemized on columns.*

203            *Q.      Any – do you disagree with anything else or do you wish to comment on anything else in that passage?*  
                   *A.      I think I generally agree that it’s something that you have to bear in mind, that there is a possibility that compounds can racemize on that column.*

[55] Thus, the '653 patent seeks to address the effective separation of omeprazole into its enantiomers. The patent does not say, however, that in so doing, interpatient variability will be addressed in some improved way.

d) **What is the solution offered to that problem by the patent?**

[56] The solution offered by the patent set out at page 2 where it is stated that a process for separating the enantiomers on a large scale has been devised and that the optically pure enantiomers can be characterized:

*The present invention in a further aspect provides a novel method of preparing the novel compounds of the invention in large scale. This novel method can also be used in large scale to obtain single enantiomers of omeprazole in neutral form.*

*There is no example known in the prior art of any isolated or characterized salt of optically pure omeprazole, i.e. single enantiomers of omeprazole in either of any isolated or characterized salt of any optically pure omeprazole analogue.*

[57] Proceeding from page 2 and following is a detailed description of the product to be obtained.

That product is discussed in detail at pages 4 and 4a:

*With the expression "optically pure Na<sup>+</sup> salts of omeprazole" is meant the (+)-enantiomer of omeprazole Na-salt essentially free of the (-)-enantiomer of omeprazole Na-salt and the (-)-enantiomer essentially free of the (+)-enantiomer, respectively. Single enantiomers of omeprazole have hitherto only been obtained as syrups and not as crystalline products. By means of the novel specific method according to one aspect of the invention by preparing the single enantiomers of omeprazole, the salts defined by the present invention are easy to obtain. In addition, the salts, however not the neutral forms, are obtained as crystalline products. Because it is possible to purify optically impure salts of the enantiomers of omeprazole by crystallisation, they can be obtained in very high optical purity, in some instances  $\geq 99.8\%$  enantiomeric excess (e.e.)*

*even from an optically contaminated preparation. Moreover, the optically pure salts are stable towards racemisation both in neutral pH and basic pH, which was surprising since the known deprotonation at the carbon atom between the pyridine ring and the chiral sulphur atom was expected to cause racemisation under alkaline conditions. This high stability towards racemisation makes it possible to use a single enantiomeric salt of the invention in therapy.*

*The specific method of preparation of the single enantiomers of omeprazole is a further aspect of the invention as mentioned above and it can be used to obtain the single enantiomers of omeprazole in neutral form (sic) as well as the salts thereof.*

*The compounds according to the invention may be used for inhibiting gastric acid secretion in mammals and man. In a more general sense, the compounds of the invention may be used for the treatment of gastric acid-related diseases and gastrointestinal inflammatory diseases in mammals and man, such as gastric ulcer, duodenal ulcer, reflux esophagitis and gastritis. Furthermore, the compounds may be used for treatment of other gastrointestinal disorders where gastric antisecretory effect is desirable e.g. in patients on NSAID therapy, in patients with gastrinomas, and in patients with acute upper gastrointestinal bleeding.*

[58] The process is described in detail at pages 5 to 8 of the '653 patent, and the formulation of the resulting product and its dosage forms at pages 8 and 9. Eleven examples follow at pages 9a to 17. From pages 17 to 21, various pharmaceutical formulations are exemplified.

[59] The description of the '653 patent concludes at page 21 with a discussion that the resulting product is resistant to racemisation:

*Stability towards racemization at different pHs*

*The stability of the optically pure compounds of the invention towards racemisation has been measured at low concentrations in refrigerator in aqueous buffer solutions at pH 8, 9.3, 10 and 11.2. The stereochemical stability was measured by comparing the optical purity for the (-)-isomer of 5-methoxy-2-[[[4-methoxy-3, 5-dimethyl-2-pyridinyl)-methyl]sulfinyl]-1H-benzimidazole in buffer solution immediately after dissolving and after several days. The*

*measurement was performed by chromatography on an analytical chiral column. The surprising high stereochemical stability in alkaline conditions for the compounds of invention is exemplified by the fact that no racemisation for the test compound was obtained at pH 11.2 even after 21 days. At pH 8, 9.3 and 10, the chemical degradation of the compound is more apparent which makes the racemisation measurement more difficult to perform, however at none of these pH values a detectable racemisation was obtained after 16 days.*

*In another racemisation experiment with the optically pure compounds of the invention, an aqueous phosphate buffer solution (pH=11) of the (+)-isomer of 5-methoxy-2-[[[4-methoxy-3, 5-dimethyl-2-pyridinyl)-methyl]sulfinyl]-1H-benzimidazole ( $c=10^{-5}M$ ) was warmed for 26 hours at 37°C without any racemization at all being observed.*

[60] Thus, the solution presented is an improved process for preparing a highly optically pure omeprazole enantiomer of omeprazole and its salts, which is stable as against racemisation. Omeprazole, and its salts, can be formulated into pharmaceutical preparations. There is no information as to whether these pharmaceutical preparations made from purified enantiomers are more or less effective than omeprazole itself, or whether the issue of interpatient variability is addressed by the enantiomer so produced. There is no discussion as to how a particular purity level affects the therapeutic utility of the final product.

e) **What is the proper construction of claim 8?**

[61] The parties have reduced the issues to validity of claim 8 of the '653 patent. That claim is a dependent claim, that is, it incorporates by reference terms appearing in the earlier claims 1 to 6;

therefore, I repeat all of claims 1 to 8 (excluding claim 7 which has been dropped from contention)

as follows:

1. *An optically pure compound characterized in that the compound is a  $\text{Na}^+$ ,  $\text{Mg}^{2+}$ ,  $\text{Li}^+$ ,  $\text{K}^+$ ,  $\text{Ca}^{2+}$  or  $\text{N}^+(\text{R})_4$  salt of (-)-5-methoxy-2-[[[4-methoxy-3, 5-dimethyl-2-pyridinyl) methyl]-sulfinyl]-1H-benzimidazole, where R is an alkyl group with 1-4 carbon atoms.*
  2. *A compound according to claim 1 characterized in that it is in solid state form.*
  3. *A compound according to claim 2 characterized in that it is in crystalline form.*
  4. *A compound according to claim 1, 2 or 3 characterized in that it is a  $\text{Na}^+$ ,  $\text{Mg}^{2+}$ ,  $\text{Li}^+$ ,  $\text{K}^+$ ,  $\text{Ca}^{2+}$  or  $\text{N}^+(\text{R})_4$  salt of (-)-5-methoxy-2-[[[4-methoxy-3, 5-dimethyl-2-pyridinyl) methyl]-sulfinyl]-1H-benzimidazole.*
  5. *A compound according to claim 1, 2 or 3 characterized in that it is the  $\text{Mg}^{2+}$  salt of (-)-5-methoxy-2-[[[4-methoxy-3, 5-dimethyl-2-pyridinyl) methyl]-sulfinyl]-1H-benzimidazole.*
  6. *A compound according to claim 1 characterized in that it is the  $\text{Na}^+$  salt of (-)-5-methoxy-2-[[[4-methoxy-3, 5-dimethyl-2-pyridinyl) methyl]-sulfinyl]-1H-benzimidazole in its crystalline form.*
- ...
8. *A compound according to any one of claims 1 to 6 having an optical purity of 99.8% or greater.*

[62] The complex chemical of the formula, as set out in claims 1, 5 and 6 is commonly referred to in the evidence simply as esomeprazole or (-)-omeprazole. The most commonly referred to salt is the Mg or magnesium salt of claim 5. Thus, claim 8 can be rewritten as follows:

8. *A salt (e.g. magnesium) of esomeprazole having an optical purity of 99.8% or greater.”*

[63] Two issues with respect to the construction of claim 8 have arisen:

1. What is the meaning of “having an optical purity of 99.8% or greater?”
2. Is there implicit in claim 8 a promise of utility, and what is that promise?

[64] As to the meaning of “having an optical purity of 99.8% or greater”, there are, in this particular field of science, two different ways of expressing optical purity of a sample of an enantiomeric compound. One way is to express optical purity in absolute terms; the other way is to express purity in terms of the excess of one enantiomer over the other, enantiomeric excess or (ee).

Dr. Collicott expressed the matter this way at paragraph 69 of his affidavit (Record, page 5671):

*...As I have noted above, “optical purity” per se is sometimes used to express purity in absolute terms, thus an optical purity of 98% or greater could refer to a material in which there is 98% or more esomeprazole and no more than 2% (+)-omeprazole. Also as noted, optical purity can be understood to mean purity in terms of enantiomeric excess (as, for instance, in Examples 1 to 5 of the ‘653 patent, which describe the optical purities of the sodium and magnesium salts of esomeprazole and (+)-omeprazole in terms of “optical purity (e.e.)”).*

[65] AstraZeneca put the issue as to the two different ways to express purity this way at paragraph 11 of the memorandum of Argument:

*11. Just as a compound may be more or less chemically pure, it may be more or less optically pure. Optical purity refers to the degree of purity of a sample of one enantiomer relative to the presence of the other enantiomer. It can be expressed as absolute purity or enantiomeric purity (the percentage of the particular enantiomer in the sample) or as enantiomeric excess (also written “ee”; representing the difference between the amount of the particular enantiomer of interest and the other enantiomer).*

[66] To address the way things are expressed when claim 8 uses the term “optical purity” of 99.8%; if that expression means absolute purity, then there are two enantiomers present, the (-) or S (es) enantiomer comprises 99.8% and the (+) enantiomer 0.2%. If the expression means enantiomeric excess (ee), that means there is 99.8% more of the (-) enantiomer than of the (+) enantiomer. To do the math, 99.6% (ee) means 99.8% absolute.

[67] As it turns out, the other issues in this case do not turn on whether the purity is expressed one way or the other; however, the meaning of other claims not at issue here may depend on that expression.

[68] The arguments for the parties are simple. AstraZeneca argues that throughout the description of the '653 patent, whenever a percentage figure is given for optical purity, it is always expressed as enantiomeric excess (ee). Each of Examples 1 through 5 express optical purity in this way. Nowhere in the description does the other way of expressing it appear. Thus, argues AstraZeneca, the informed person reading claim 8 in a purposive way would conclude that the claims was to be read in terms of enantiomeric excess (ee).

[69] Apotex argues that, given that there are two ways of expressing optical purity, and given that the patentee clearly knew how to express the matter one of those ways, using (ee) in the description, the other way, absolute purity, must have been intended when (ee) was omitted in the claims.

[70] I agree with AstraZeneca's interpretation; 99.8% should be read as meaning optical purity expressed in terms of enantiomeric excess. A person skilled in the art in reading claim 8 would

know that optical purity can be expressed as a percentage in one of two ways. That person would wish to read the claim in an “informed and purposive” way, looking at the whole of the disclosure and the claims (*Whirlpool Corp. v. Camco Inc.*, [2007] 2 S.C.R. 1067 at paragraph 49). In so doing, the person skilled in the art would recognize that the percentage of optical purity in claim 8 was intended to be expressed in terms of enantiomeric excess (ee).

[71] The second issue is whether there is implicit in claim 8 a provision as to utility. Clearly, there is nothing respecting utility expressly stated. A contrast can be made with claims 25 to 28 of the ‘653 patent which clearly state a therapeutic use.

[72] The Patent Act, *supra*, section 2, describes an “invention” as something that is new and useful. Usefulness, or utility, in this sense, has been discussed by the Supreme Court of Canada in *Colsolboard Inc. v. MacMillan Bloedel (Saskatchewan) Ltd.* (1981), 56 C.P.R. 145 per Dickson J. at pp. 160-161:

*In my respectful opinion the Federal Court of Appeal erred also in holding that s. 86(1) requires distinct indication of the real utility of the invention in question. There is a helpful discussion in 29 Hals., 3<sup>rd</sup> ed., p. 59, on the meaning of “not useful” in patent law. It means “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”. There is no suggestion here that the invention will not give the result promised. The discussion in Halsbury, *ibid.*, continues:*

*...the practical usefulness of the invention does not matter, nor does its commercial utility, unless the specification promises commercial utility, nor does it matter whether the*

*invention is of any real benefit to the public, or particularly suitable for the purposes suggested.*

*and concludes [at p. 60]:*

*...it is sufficient utility to support a patent that the invention gives either a new article, or a better article, or a cheaper article, or affords the public a useful choice.*

*(Footnotes omitted.)*

*Canadian law is to the same effect. In Rodi & Wienenberger Aktiengesellschaft v. Metalliflex Ltd. (1959), 32 C.P.R. 102, 19 Fox Pat C. 49, [1960] que. Q.B. 391n; affirmed in the Court 35 C.P.R. 49, [1961] S.C.R. 117, 21 Fox Pat. C. 95, the Quebec Court of Appeal adopted at p. 107 C.P.R., p. 53 Fox Pat. C., the following quotation from the case of Unifloc Reagenta Ltd. v. Newstead Colliery Ltd. (1943), 60 R.P.C. 165 at p. 184:*

*“If and when used in accordance with the directions contained in the specification, the promised results are obtained, the invention is useful in the sense in which that term is used in the patent law. The question to be asked is whether, if you do what the specification tells you to do, you can make or do the thing which the specification says you can make or do.”*

*Although (i) s. 86(1) requires the inventor to indicate and distinctly claim the part, improvement or combination which he claims as his invention and (ii) to be patentable an invention must be something new and useful (s.2), and not known or used by any other person before the applicant invented it (s. 28(1)(a), I do not read the concluding words of s. 36(1) as obligating the inventor in his disclosure or claims to describe in what respect the invention is new or in what way it is useful. He must say what it is he claims to have invented. He is not obliged to extol the effect or advantage of his discovery, if he describes his invention so as to produce it.*

[73] Where there is a new compound, utility does not need to be included in the claim, so long as it is described in the descriptive portion of the patent; see *Janssen-Ortho Inc. v. Novopharm Limited*, 2006 FC 1234 at paragraph 96:

**96** *The claim does not address medical properties or uses, nor does it need to. Where the compound is new, it is sufficient that its*

*utility is set out in the specification it need not be included in the claim. (Monsanto Canada Inc. v. Schmeiser (2001), 12 C.P.R. (4th) 204 (F.C.) at para. 26, aff'd (2006), 21 C.P.R. (4th) 1 (F.C.A.) at paras. 41 to 46, aff'd, [2004] 1 S.C.R. 902; Aventis Pharma Inc. v. Apotex Inc. (2006), 43 C.P.R. (4th) 161 (F.C.) at para. 82, aff'd (2006), 46 C.P.R. (4th) 401 (F.C.A.))*

[74] That, however, is directed to a “new compound”. Where there is a new use for an old compound, that new use must be set out in the claims (see e.g. *Shell Oil Co. v. Canada (Commissioner of Patents)*, [1982] 2 S.C.R. 536).

[75] In the present case, claim 8 is not directed to a new compound; it is directed to a previously known compound having a particular purity. No particular use of that compound is expressed in the claim. Thus, so far as claim construction is concerned, we have only a known compound having a particular purity claimed. The issue of utility will arise later in considering sound prediction and utility.

[76] Thus, as a matter of construction, claim 8 reads as follows:

“8. A salt (e.g. magnesium) of esomeprazole having an optical purity of 99.8% (ee) or greater.”

f) **Who bears the burden of proof?**

[77] There is no doubt that, in respect of allegations as to invalidity by a generic in a Notice of Allegation served in the context of the *NOC Regulations*, the burden of proof in an application to the Court such as the one at present is as expressed at paragraph 32 of *Pfizer Canada Inc. v. Canada (Minister of Health)*, 2008 FC 11, 69 C.P.R. (4<sup>th</sup>) 191:

*32 I do not view the reasoning of the two panels of the Federal Court of Appeal to be in substantial disagreement. Justice Mosley of this Court reconciled these decisions in his Reasons in Pfizer Canada Inc. v. Apotex Inc., [2007] F.C.J. No. 1271, 2007 FC 971 at paragraphs 44 to 51. What is required, when issues of validity of a patent are raised:*

- 1. The second person, in its Notice of Allegation may raise one or more grounds for alleging invalidity;*
- 2. The first person may in its Notice of Application filed with the Court join issue on any one or more of those grounds;*
- 3. The second person may lead evidence in the Court proceeding to support the grounds upon which issue has been joined;*
- 4. The first person may, at its peril, rely simply upon the presumption of validity afforded by the Patent Act or, more prudently, adduce its own evidence as to the grounds of invalidity put in issue.*
- 5. The Court will weigh the evidence; if the first person relies only on the presumption, the Court will nonetheless weigh the strength of the evidence led by the second person. If that evidence is weak or irrelevant the presumption will prevail. If both parties lead evidence, the Court will weigh all the evidence and determine the matter on the usual civil balance.*
- 6. If the evidence weighed in step 5 is evenly balanced (a rare event), the Applicant (first person) will have failed to prove that the allegation of invalidity is not justified and will not be entitled to the Order of prohibition that it seeks.*

[78] I admit that in *Merck & Co. Inc. v. Pharmascience Inc.*, 2010 FC 510 at paragraphs 27 and 181 I got it twisted around so that it came out wrong. Let me be quick to say that the result in *Merck* remains the same, invalidity as to obviousness was not shown, Merck had satisfied me that the allegations as to invalidity for obviousness were not justified. NOC proceedings are arcane and

complex. I have advised the parties in *Pharmascience* that I will rewrite paragraphs 27 and 181 of that decision as follows:

*[27] In the present case, Pharmascience has made extensive allegations and both parties have led evidence as to the validity of claim 5 of the '457 patent. Subject to the arguments raised by Merck as to whether Sound Prediction/Overbreadth was raised in the Notice of Allegation, I must decide the issue of validity before me on the weight of the evidence and arguments presented. If that weight is evenly balanced in respect of any allegation, I must find that particular allegation made by Pharmascience to be justified.*

...

*[181] In the present case before me, I find, on the evidence, particularly that of Doctor Russell, that because of the Harris and Thigpen papers, a researcher would be discouraged from pursuing research in that area. In other words, the "motivation" would be lost. Thus, it has been proven that the allegations that claim 5 of the '457 Patent was not obvious was not justified.*

[79] Having discussed all of the above, I turn to the grounds alleged by Apotex as to invalidity.

## ISSUES AS TO VALIDITY

### 1. Lack of Sound Prediction as to Utility

[80] Apotex's Notice of Allegation alleged invalidity of all claims then relevant (claims 1 - 5, 7, 8 and 24 - 29) on several grounds, beginning at page 11 of that Notice (Record, page 855). Among those grounds was Lack of Sound Prediction and Insufficiency, commencing at page 50 - 51 (Record, pages 894 – 895):

#### 6. *Lack of Sound Prediction and Insufficiency*

*Owing to the absence of any data or disclosure in the specification of the '653 Patent as to the nature and extent of the "improved pharmacokinetic or metabolic properties which will give an improved therapeutic profile such as a lower degree of interindividual variation" other than the generic statement on page*

*1, lines 18-22 of the specification, and as claimed in claims 28 and 29 of the '653 Patent, Apotex alleges that the purported filing date (May 27, 1994), any sound basis on which to predict the above noted properties for any of the purportedly novel salts of esomeprazole, including magnesium esomeprazole, over and above those that would have been expected for the previously known omeprazole, salts of omeprazole including magnesium omeprazole, and the previously known single enantiomers of omeprazole in their salt or non-salt form. Should you assert that the purported inventors did have the ability to make such a prediction based on experimental data not disclosed in the patent, Apotex further alleges that the requirement properly to disclose such data has not been met, and that the specification is therefore invalid as being insufficient, and thus contrary to subsection 27(3) of the patent Act.*

*The concept of utility is incorporated into the definition of "invention" in section 2 of the patent Act through the term "useful". Section 2 of the patent Act defines "invention" as meaning any new and useful art, process, machine, manufacture or composition of matter. In order for there to have been an invention, the purported inventors must have, as at the relevant date, demonstrated utility or have soundly predicted the utility of the subject-matter of the claims as at that date. Utility, in the patent sense, means that the invention will do what the specification promises that it will do. The doctrine of sound prediction is discussed in *Apotex Inc. et al, v. Wellcome Foundation Limited et al*, 2002 SCC 77, File No. 28287, reported as [2002] 4 S.C.R. 153. In particular, it was noted that the doctrine of sound prediction has three components:*

- (1) There must be a factual basis for the prediction;*
- (2) The inventor must have at the date of the patent application 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.*

*Apotex alleges that even if components (1) and (2) of the doctrine of sound prediction has been met by the purported inventors, which is denied, that component (3), that of proper disclosure, has not been met. In particular, Apotex alleges that the general statements as to "improved pharmacokinetic or metabolic properties which will give an improved therapeutic profile such as a lower degree of interindividual variation" for the purportedly novel compounds of*

*the invention does not amount to a proper disclosure of any such properties.*

*In support of this allegation, Apotex relies on the description provided in the '653 patent, which is devoid of any advantages to be gained through the use of the purportedly novel claimed salts of esomeprazole over those of the racemate or (+)-enantiomer. The '653 Patent itself notes that the most preferred compounds of the invention include the sodium and magnesium salts of both the (+)- and (-)-enantiomers.*

[81] As discussed in respect of claim construction, a patented invention must be “new and useful”.

If the invention lies in a new compound, the utility must be disclosed in the descriptive part of the patent; it may or may not be expressly included in the claims. If the invention lies in a new use for an old compound, the utility must be included in the claim.

[82] Here we are dealing only with claim 8 of the '653 patent. That claim is for the salts of esomeprazole having a certain high level of purity. The utility is stated at page 1 of the patent:

*It is desirable to obtain compounds with improved pharmacokinetic and metabolic properties which will give an improved therapeutic profile such as a lower degree of interindividual variation. The present invention provides such compounds, which are novel salts of single enantiomers of omeprazole.*

[83] That utility is, according to what is set out at page 4 of the patent, made possible by one of the results of having a high purity of the esomeprazole, namely, stability towards racemisation:

*Moreover, the optically pure salts are stable towards racemisation both in neutral pH and basic pH, which was surprising since the known deprotonation at the carbon atom between pyridine ring and the chiral sulphur atom was expected to cause racemisation under alkaline conditions. This high stability towards racemisation makes it possible to use a single enantiomeric salt of the invention in therapy.*

[84] It is important to distinguish between the utility promised by the patent- “*improved therapeutic profile, such as lower degree of interindividual variation*” “and the particular property that makes that possible “*high stability towards racemisation*”.

[85] Nowhere in the patent, whether in the Examples or otherwise, is any information given to the person skilled in the art as to whether, in fact, the highly pure esomeprazole salt does give an improved therapeutic profile such as a lower degree of interindividual variation. There is no evidence from any witness to say that there is anything in the disclosure of the ‘653 patent that would inform a person skilled in the art that the purified esomeprazole salt fulfills this promise. Counsel for AstraZeneca argued that all that was required was that an alternative to racemic omeprazole be provided not whether it is an improvement. This argument ignores the promise of the patent as set out in the portion recited above at page 1 that the resulting product would provide “*an improved therapeutic profile*”.

[86] There is in evidence the affidavit of Dr. Andersson stating that there was ongoing research conducted at AstraZeneca commencing in 1987 directed toward developing a proton pump inhibiting drug that would be more effective and be less variable (Andersson affidavit, paragraphs 15 to 35) (Record, pages 437 – 442). I repeat paragraphs 26 to 29 of that affidavit:

26. *Despite a lack of interest by the company, optically pure salts of enantiomers were tested in animals.*

27. *The rat studies were highly surprising. First, the enantiomers were stable against racemisation, in vivo. Second, the enantiomers behaved differently from each other, in vivo. After intraduodenal administration of the sodium salts of S-omeprazole and R-omeprazole, it was observed that the enantiomers were metabolized at substantially different rates and had substantially different*

*bioavailabilities, which correlated to different (but not statistically significant) gastric acid output.*

28. *Given these findings, the enantiomers were further tested, next in an in vitro human model in April 1993. In these studies, human liver microsomes containing CYP2C19 (i.e. corresponding to an EM) were exposed to the individual enantiomers of omeprazole. The metabolism of the enantiomers by CYP2C19, measured by tracking the levels of the corresponding 5-hydroxy omeprazole metabolite, differed by an order of magnitude between the enantiomers, with CYP2C19 metabolizing R-omeprazole 10 times more readily than esomeprazole.*

[...]

[87] The results of these studies were set out in an internal AstraZeneca report dated August 17, 1994, referred to in evidence as the Elebring report (Record, pages 1038 – 1053). That report deals with the consideration of two omeprazole enantiomers identified as H 199/18 and H 199/19; the testing on rats and on human liver microsomes. The report concludes:

[...]

[88] [...]

[89] Nothing of this work or the report appears in the '653 patent. The report was not dated until three months after the filing of the patent application in Canada and fifteen months after the priority filing in Sweden. [...]

[90] Even if claim 8 does not expressly claim utility, the claimed invention must possess utility. For example, one cannot simply prepare a compound, then claim it at various levels of purity, say 90%, 92%, 94%, 96%, etc., without stating why such purity level is useful. The invention is not

simply a molecule or a molecule of a certain purity, it must, as the Federal Court of Appeal said in *Merck & Co. v. Apotex Inc.* (1995), 60 C.P.R. (31) 356 at page 373 “inherently” possess utility:

*In my view, the appellant was in error in contending that the invention was simply chemical molecules of enalapril. Chemically speaking, that was so. But the specification of the patent, properly construed, asserts more than that. In this respect, the trial judge was entirely right when he wrote (Appeal Book, vol. I, at p.27) [p. 156 C.P.R.]:*

*[T]he patent...claims more than a molecule with a chemical formula. Rather, the claims describe several or many compounds, and several compositions, and specific uses for them, all aspects of the same invention. Enalapril may be the essence of each claim, but the claims, and the patent for the invention, are more than the chemical molecule of enalapril or of enalapril maleate.*

*Inherent in the compound, and indeed in the patent, is the purpose and utility of the compound of enalapril.*

[91] Given that the ‘653 patent promises utility in terms of improved therapeutic properties such as less interindividual variation, and given that at the time of the priority filing date of the application - and even as of the Canadian filing date there were no conclusions [...] - let alone any publicly available conclusions – did the invention have a basis for a “sound prediction” as to utility?

[92] The requirements for sound prediction are well established. The Supreme Court of Canada in *Apotex Inc. v. Wellcome Foundation Ltd.* [2002] 45 S.C.R. 153 at paragraphs 70 and 71 set these out: 1) there must be a factual basis for the prediction; 2) the inventors must have as of the date of the patent application 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:

*70 The doctrine of sound prediction has three components. Firstly, as here, there must be a factual basis for the prediction. In*

*Monsanto and Burton Parsons, the factual basis was supplied by the tested compounds, but other factual underpinnings, depending on the nature of the invention, may suffice. Secondly, the inventor must have at the date of the patent application an articulable and "sound" line of reasoning from which the desired result can be inferred from the factual basis. In Monsanto and Burton Parsons, the line of reasoning was grounded in the known "architecture of chemical compounds" (Monsanto, at p. 1119), but other lines of reasoning, again depending on the subject matter, may be legitimate. Thirdly, there must be proper disclosure. Normally, it is sufficient if the specification provides a full, clear and exact description of the nature of the invention and the manner in which it can be practised: H. G. Fox, The Canadian Law and Practice Relating to Letters Patent for Inventions (4th ed. 1969), at p. 167. It is generally not necessary for an inventor to provide a theory of why the invention works. Practical readers merely want to know that it does work and how to work it. In this sort of case, however, the sound prediction is to some extent the quid pro quo the applicant offers in exchange for the patent monopoly. Precise disclosure requirements in this regard do not arise for decision in this case because both the underlying facts (the test data) and the line of reasoning (the chain terminator effect) were in fact disclosed, and disclosure in this respect did not become an issue between the parties. I therefore say no more about it.*

*71 It bears repetition that the soundness (or otherwise) of the prediction is a question of fact. Evidence must be led about what was known or not known at the priority date, as was done here. Each case will turn on the particularities of the discipline to which it relates. In this case, the findings of fact necessary for the application of "sound prediction" were made and the appellants have not, in my view, demonstrated any overriding or palpable error.*

[93] The facts of the present case do not show that as of the priority date, May 1993, or even the Canadian filing date, May 1994, that the inventors had either a factual basis for a prediction thatesomeprazole salt of a particular purity would have the utility indicated in the patent, nor did they have an articulable and sound line of reasoning for referring such a result. Clearly, there was no proper disclosure in the patent in that respect.

[94] I find that Apotex's allegation that claim 8 is invalid for lack of sound prediction for insufficient support as to utility is justified.

2. Anticipation having regard to the state of the art and the German application DE'455

[95] German patent application DE 40 35 455 A1 (De'455) was laid open (made available to the public) May 14, 1992; that is, more than one year before the priority date of the patent application for the '653 patent at issue here, and more than two years before the filing date of the Canadian application for the '653 patent. As such it is a proper reference for purposes of anticipation from a date point of view.

[96] DE '455 discloses a method for producing what it describes as "*optically pure compounds from the diastereomers*" of a class of compounds, including omeprazole. Those optically pure compounds can be employed as active ingredients to treat gastric disorders.

At page 13, it is stated (English translation – Record, page 272):

*Commercial Utility*

*Pyridylmethylsulphinyl-1H-benzimidazoles can be resolved into their optical antipodes for the first time by the process according to the invention. The fact to be judged as particularly surprising here is that the liberation of the optically pure compounds from the diastereomers is carried out with the aid of highly concentrated mineral acids, although it is known that the pyridylmethylsulphinyl-1H-benzimidazoles are very acid-labile compounds. The compounds prepared according to the invention are employed as active ingredients in medicaments for the treatment of gastric and intestinal disorders. Reference is made, for example, to European patent 166 287 with respect to the manner of use and dosage of the active ingredients.*

[97] A process for arriving at these optically pure compounds is described. Essentially, a second position is created in the molecule about which a further stereocentre exists so that with a further twist of the stereoisomers, a diastereomer is made as an “intermediate” compound. The diastereomer is more easily separable, and converted back to the isomers. Example 5 at page 12 shows the making of the diastereomers of esomeprazole, which are described as colourless crystals with a melting point of 161°C. Example 6, using the process of Example 2, converts the diastereomers to the (+) enantiomer of omeprazole. No melting point nor any particular purity is reported.

[98] This is the process that the ‘653 patent disclosure at pages 1 and 2 describes as having problems with localized pH and heat generation, making large-scale production difficult. Nonetheless, a number of patents and scientific articles make reference to DE ‘455 as disclosing a process for separation of the enantiomers of omeprazole, including patents, and articles by the named inventors of the ‘653 patent (Here it is sufficient to refer to the undisputed documents - others were in dispute and need not be referred to - the undisputed are in the Record at pages 8010 ff; 8028 ff; 8077 ff; 8165 ff; 8172 ff). I refer to one of those, United States Patent 5,948,789 (Record, page 8010 ff), which states at columns 1 and 2:

*There are processes for resolution of different substituted 2-(2-pyridinylmethylsulphinyl)-1H-benzimidazoles disclosed in the prior art. Such resolution processes are for example described in DE 403,5455 and WO 94/27988. These processes involve synthetic steps wherein a diastereomeric mixture is synthesized from the racemate of the corresponding substituted 2-(2-pyridinylmethylsulphinyl)-1H-benzimidazoles. The diastereomers are then separated and finally one of the separated diastereomer is converted to the optically pure sulphoxide in a hydrolytic step.*

*These resolution methods involving diastomeric intermediates, suffer from at least three fundamental disadvantages namely:*

- 1) The substituted 2-(2-pyridinylmethylsulphinyl)-1H-benzimidazole, as a racemic intermediate, has to be further processed in a couple of reaction steps before the single enantiomers can be obtained.*
- 2) The resolution processes described involve complicated separation steps.*
- 3) There is a large waste of highly refined material when the unwanted stereoisomer in the form of the opposite diastomer is separated and discarded.*

[99] The point to be made in this regard is that the inventors named in the '653 patent themselves have publicly acknowledged that DE '455 discloses the separation of the enantiomers of omeprazole, albeit using a complex process in which there is a great deal of waste. They describe the resulting enantiomers as "optically pure".

[100] AstraZeneca's Counsel argues, and I accept, the following:

- The skilled person would not at once perceive or understand that DE 455 describes (-)-omeprazole or any alkaline salts with optical purity of 99.8% or greater ee.*
- DE 455 does not express optical purity numerically. This is undisputed.*
- Although DE 455 refers to the compounds as "optically pure", there is no discussion or description in DE 455 of the term. This is also undisputed.*
- DE 455 does not provide any measurement of optical purity. This is also undisputed.*

[101] The only evidence that is in the Record as to what a person skilled in the art would have understood by “optically pure” is found in the affidavit of Dr. Davies, particularly at paragraphs 87 and 88 (Record, page 793), where he opines that such a person would presume that the enantiomer would possess a 90% or more enantiomeric excess purity:

87. *The ‘455 patent application, however, describes the material obtained by the disclosed method as “optically pure”. (‘455 patent application at page 7, lines 14 to 17; claim 2). The term optically pure does not occur anywhere else in the text of the ‘455 patent. No guidance is provided as to the meaning of “optically pure.”*

88. *While a skilled person would understand by convention that the term “optically pure” in the ‘455 patent application suggests 95% or more enantiomeric purity (90% enantiomeric excess), without any method or evidence being specified, the claim is without substance.*

[102] Apotex argues that Dr. Davies did not read “*optically pure*” as part of the whole of the phrase in which it is used in DE ‘455, namely, “*configurationally homogeneous, optically pure*”. I have read Dr. Davies’ cross-examination on the point and find no reason that would suggest that this would have made a difference. Apotex offered no evidence of its own as to what “*optically pure*”, with or without the modifier, “*configurationally homogeneous*”, would have meant to a person skilled in the art in 1993.

[103] Thus, what DE ‘455 discloses, as may be relevant to claim 8, is the (+) enantiomer of omeprazole useful in treating gastric problems having an “optical purity” of at least 90% (ee). The parties made no issue that to disclose the (+) enantiomer is to disclose equally the (-) enantiomer of esomeprazole. Further, no serious argument was raised as to the salts of omeprazole and enantiomers as DE ‘455 also discloses the salts (page 2, line 19; page 10, line 2).

[104] A disclosure in and of itself may be sufficient to constitute anticipation, that is, that there is nothing novel in the invention as claimed. However, in particular with respect to chemistry, a disclosure must be sufficient to “enable” the claimed invention to be made or used or carried out as the case may be. This is called “disclosure and enablement” , as discussed by the Supreme Court of Canada in *Apotex Inc. v. Sanofi-Synthelabo Canada Inc.*, [2008] 3 S.C.R. 265. I repeat what Rothstein J. for the Court wrote at paragraphs 23, 25 to 27 and 30 of that case:

*23 For the reasons that follow, and in light of recent jurisprudence, I am of the respectful opinion that the applications judge overstated the stringency [page279] of the test for anticipation that the "exact invention" has already been made and publicly disclosed.*

...

*25 He explains that the requirement of prior disclosure means that the prior patent must disclose subject matter which, if performed, would necessarily result in infringement of that patent, and states, at para. 22:*

- *If I may summarise the effect of these two well-known statements [from *General Tire and Hills v. Evans*], the matter relied upon as prior art must disclose subject matter which, if performed, would necessarily result in an infringement of the patent... . 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. 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.*

*26 If the disclosure requirement is satisfied, the second requirement to prove anticipation is [page280] "enablement" which means that the person skilled in the art would have been able to perform the invention (para. 26). Lord Hoffmann held that the test for enablement for purposes of anticipation was the same as the test for sufficiency under the relevant United Kingdom*

*legislation. (Enablement for the purposes of sufficiency of the patent specification under the Canadian Patent Act, s. 34(1)(b) of the pre-October 1, 1989 Act, now s. 27(3)(b), is not an issue to be decided in this case and my analysis of enablement is solely related to the test for anticipation. The question of whether enablement for purposes of sufficiency is identical in Canada is better left to another day.)*

*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.*

...

*30 Two questions now must be answered: (1) what constitutes disclosure at the first stage of the test for anticipation, and (2) how much trial and error or experimentation is permitted at the enablement stage?*

[105] As to enablement, Rothstein J. wrote at paragraph 33:

*33 What amount of trial and error or experimentation is permitted before a prior disclosure will not constitute enabling disclosure? Certainly, if the applications judge finds that an inventive step was required to get to the invention of the second patent, the specification of the first patent will not have provided enabling disclosure. But even if no inventive step is required, the skilled person must still be able to perform or make the invention of the second patent without undue burden.*

[106] Thus, the question here is, given that DE '455 describes a process for separating the enantiomers of omeprazole (and salts) into "optically pure" fractions, does the description, particularly Examples 5 and 6 (incorporating Examples 1 and 2) "enable" what is claimed in claim 8, a purity of 99.8% (ee) or greater?

[107] There was considerable procedural wrangling before this matter was heard as to whether certain evidence could be filed and whether AstraZeneca could file certain reply evidence.

However, as the Record has emerged, the Court has in evidence as provided by Apotex of certain experiments conducted by Dr. Bihovsky where he purports to replicate Examples 5 and 6 of DE '455 as it would have been done in 1993, and Dr. Batey, who analyzed the resulting samples.

AstraZeneca has filed the evidence of Dr. Larsson, who testified as to certain tests conducted by AstraZeneca in 1993, which he says failed to produce results. AstraZeneca also filed the evidence of Dr. Kohl and Dr. Senn-Bilfinger, the persons named as inventors in DE '455, attesting as to the results that were obtained at the time they performed the work exemplified in Examples 5 and 6.

#### THE BIHOVSKY / BATEY REPLICATIONS OF DE '455

[108] In dealing with whether DE '455 enabled a person skilled in the art to make 99.8% (ee) pure esomeprazole, Apotex submitted the evidence of Drs. Bihovsky and Batey, both as fact witnesses. Each was cross-examined.

[109] AstraZeneca filed evidence from the two persons named as inventors of DE '455, Drs. Kohl and Senn-Bilfinger, as well as evidence from Dr. Larsson as to work done in 1993 at AstraZeneca by Dr. Niman in an endeavour to replicate DE '455.

[110] The evidence of Drs. Bihovsky and Batey is, essentially, that Dr. Bihovsky prepared samples in accordance with the examples of DE '455 which were forwarded to Dr. Batey for analysis as to purity. Dr. Batey analyzed two samples; one he found to have a purity (ee) of 99.6%  $\pm$  0.1; the other, he found to have a purity (ee) of 99.7%  $\pm$  0.1. The latter sample, therefore, would come

within the limit set by claim 8 of 99.8%, given the standard deviation of  $\pm 0.1\%$  (Batey affidavit, paragraphs 34 and 40, Record, pages 5183 – 5184).

[111] No question has arisen concerning Dr. Batey's analysis of the samples. AstraZeneca challenges the work of Dr. Bihovsky, who made the samples. These challenges, however, do not arise from any evidence tendered by witnesses; only from argument of Counsel.

[112] To be more precise as to what Dr. Bihovsky did, his evidence (Record, pages 5287 to 5306; Exhibits, pages 5307 to 5450; cross-examination, pages 6664 to 6867) shows the following:

- He obtained racemic omeprazole magnesium from an Apotex source, inspected and analyzed it to confirm that this is what it was.
- He converted racemic omeprazole magnesium to racemic omeprazole sodium and tested it to confirm that this is what it was.
- He prepared a (+)-fenchyl chloromethyl ether, which is needed to follow Example 5 of DE '455, tested it and confirmed that that is what it was.
- He repeated Example 5 (which incorporated Example 1) of DE '455 and obtained (+)-fenchyloxymethyl-(+)-omeprazole, tested it and confirmed that is what it was.

- He repeated Example 6 (which incorporates, by reference, Example 2) of DE '455. In so doing, the pH was at 7 when the sodium hydroxide was added. He adjusted the pH to 8 by adding sodium carbonate. A "lilac-coloured amorphous solid" was produced, which he took to be (+)-omeprazole. Three fractions of product were obtained, two of which contained this solid. The solid was tested and confirmed to be (+)-omeprazole. This (+)-omeprazole was sent to Dr. Batey for purity analysis.
- The Examples 5 and 6 were run a second time. In running Example 6 from the product of Example 5, the initial pH this time was 1, which was adjusted in two samples with sulphuric acid and in a third sample, with phosphoric acid, to 7.5 pH. The samples from the first two (sulphuric acid) runs were not tested as they appeared to contain contamination of some kind. Samples from the third run (phosphoric acid) were retained and tested and found to contain (+)-omeprazole. These samples were sent to Dr. Batey.

[113] AstraZeneca takes issue with the procedures followed by Dr. Bihovsky in the following respects:

- The samples taken from the first run in which Dr. Bihovsky attempted to replicate Examples 5 and 6 of DE '455 were tested by Dr. Batey and fell below 99.8% (ee) purity and are, therefore, irrelevant.
- From the second run, the first two attempts in which the pH was adjusted using sulphuric acid, resulted in a product that was discarded without testing. AstraZeneca characterizes this as a failure. The third attempt was made by switching to phosphoric acid, something not set out in DE '455.

- The samples obtained were, in any event, all impure, containing visible impurities.

[114] AstraZeneca further argues that the evidence of Dr. Larsson stating that his staff, in particular Dr. Niman, in 1993, when DE '455 became published, attempted three times to replicate Examples 5 and 6, and were unsuccessful in achieving 99.8% (ee) purity of (+)-omeprazole (Larsson affidavit, paragraphs 22 - 32; Record, pages 228 - 232).

[115] Finally, AstraZeneca relies on the evidence of the named inventors of DE '455 themselves, Drs. Kohl and Senn-Bilfinger. They made three attempts in 1990 to obtain (+)-omeprazole. Their records show that the intermediate (Example 5) was produced with a purity of 91 to 92% (ee). The intermediate was converted using the procedure of Example 6 to produce some (+)-omeprazole in the form of a brown viscous oil. Its purity was apparently not measured. (Kohl affidavit, paragraphs 70 – 104; Record, pages 147 - 150).

[116] Apotex, on the other hand, argues that Dr. Bihovsky's work was that of simple trial and error of the kind expected of a person of ordinary skill in the art, and that he was successful in obtaining a sample of (+)-omeprazole within the purity specified by claim 8. Apotex argues that Dr. Bihovsky made routine adjustments in substituting phosphoric acid for sulphuric acid; Examples 6 and 2 of DE '455 do not specify what acid to use. They simply say to adjust the pH.

[117] Apotex argued that Dr. Kohl's evidence was largely hearsay; the work was done by others – a point I have already dealt with. The analysis of the intermediate was made only recently when the

sample was seventeen years old. Dr. Collicott says that the sample would have degraded over time (affidavit, paragraph 163; Record, page 5694).

[118] As to the work done at AstraZeneca by Dr. Niman, as testified to by Dr. Larsson, Apotex argued that this evidence is hearsay – this point has already been discussed in these Reasons. Apotex further argues, through Dr. Heathcock (affidavit, paragraphs 183 – 195; Record, pages 5753 – 5757), that Dr. Niman did not accurately follow DE ‘455; the work was done in a hurry and was substandard.

[119] I am satisfied, given all the evidence on the point, that those following the Examples 5 and 6 (incorporating Examples 1 and 2) of DE ‘455 could make (+)-omeprazole and could, on occasion, make it of an optical purity within the 99.8% (ee) range of claim 8 of the ‘653 patent. I am also satisfied that it was not inevitable that (+)-omeprazole of this purity could always, or even usually, be achieved. It could be achieved sometimes.

[120] I have no doubt that the persons named as inventors by AstraZeneca in the ‘653 patent were really seeking a better method for making omeprazole enantiomers than that disclosed in DE ‘455. They were seeking a method that could be used commercially. They seem to have done that. The process claims of the ‘653 patent are not at issue here. The question is whether the resulting product, a known product, esomeprazole, with a particularly high purity, 99.8% (ee), itself can be properly claimed as a separate claim in the patent.

[121] Counsel have each referred to the decision of the Supreme Court of Canada in *Sanofi-Synthelabo Canada Inc., v. Apotex Inc.*, 2008 SCC 61, [2008] 3 S.C.R. 265, and in particular, to the portions of those Reasons where Rothstein J. for the Court discussed the requirement that, to be an anticipation, a prior disclosure must “enable” a person skilled in the art to do or make what the patent at issue now claims, even if trial and error to some degree is required, so long as it is without “undue burden”. He wrote at paragraphs 33 and 37:

*[33] What amount of trial and error or experimentation is permitted before a prior disclosure will not constitute enabling disclosure? Certainly, if the applications judge finds that an inventive step was required to get to the invention of the second patent, the specification of the first patent will not have provided enabling disclosure. But even if no inventive step is required, the skilled person must still be able to perform or make the invention of the second patent without undue burden.*

...

*[37] Drawing from this jurisprudence, I am of the opinion that the following factors should normally be considered. The list is not exhaustive. The factors will apply in accordance with the evidence in each case.*

- 1. Enablement is to be assessed having regard to the prior patent as a whole including the specification and the claims. There is no reason to limit what the skilled person may consider in the prior patent in order to discover how to perform or make the invention of the subsequent patent. The entire prior patent constitutes prior art.*
- 2. The skilled person may use his or her common general knowledge to supplement information contained in the prior patent. Common general knowledge means knowledge generally known by persons skilled in the relevant art at the relevant time.*
- 3. The prior patent must provide enough information to allow the subsequently claimed invention to be performed without undue burden. When considering whether there is undue burden, the nature of the invention must be taken into account. For example, if*

*the invention takes place in a field of technology in which trials and experiments are generally carried out, the threshold for undue burden will tend to be higher than in circumstances in which less effort is normal. If inventive steps are required, the prior art will not be considered as enabling. However, routine trials are acceptable and would not be considered undue burden. But experiments or trials and errors are not to be prolonged even in fields of technology in which trials and experiments are generally carried out. No time limits on exercises of energy can be laid down; however, prolonged or arduous trial and error would not be considered routine.*

4. *Obvious errors or omissions in the prior patent will not prevent enablement if reasonable skill and knowledge in the art could readily correct the error or find what was omitted.*

[122] I followed the *Sanofi* decision in *Abbott Laboratories v. Canada (Minister of Health)* (2008), 2008 FC 1359, 71 C.P.R. (4<sup>th</sup>) 237, together with a later reported English decision and a later decision of the Supreme Court of Canada. I concluded at paragraph 75:

*75 To summarise the legal requirements for anticipation as they apply to the circumstances of this case:*

- 1. For there to be anticipation there must be both disclosure and enablement of the claimed invention.*
- 2. 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.*
- 3. 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.*
- 4. The disclosure when carried out may be done without a person necessarily recognizing what is present or what is happening.*
- 5. 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.*

6. *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.*

7. *If a person carrying out the prior disclosure would infringe the claim then the claim is anticipated.*

[123] What we are faced with in the present case is a piece of a prior art, DE '455, which discloses a process for making "optically pure" omeprazole enantiomer. On some occasions, that purity would reach 99.8% (ee); on other occasions (e.g. the first Run by Dr. Bihovsky) a lower purity was achieved. On other occasions, nothing worth the trouble of testing was achieved (Bihovsky Run 2 first two attempts; Larsson/ Niman at AstraZeneca ; Kohl/Senn-Bilfinger).

[124] On the basis of this evidence, I find that, to use the words of Lord Hoffman in *Synthon BV v. SmithKline Beecham plc*, [2006] 1 All E.R. 685, [2005] UKHL 59, at paragraph 22, to perform DE '455 would not "necessarily result" in an infringement of claim 8.

**[22]** If I may summarise the effect of these two well-known statements, the matter relied upon as prior art must disclose subject matter which, if performed, would necessarily result in an infringement of the patent. That may be because the prior art discloses the same invention. In that case there will be no question that performance of the earlier invention would infringe and usually it will be apparent to someone who is aware of both the prior art and the patent that it will do so. 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' (see *Merrell Dow Pharmaceuticals Inc v H N Norton & Co Ltd* (1995) 33 BMLR 201 at 213, [1996] RPC 76 at 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.

[125] I do not equate “necessarily result” with “always result” or “inevitably result”; however, given the evidence in the present case, I find that to practice DE ‘455 would at best only occasionally result in a product with the purity level stipulated in claim 8. On this basis, I find no enablement such as would support an allegation of anticipation. The allegation as to anticipation is not justified.

2. Obviousness having regard to the state of the art, DE ‘455 and the Erlandsson article

[126] I have reviewed the “state of the art” earlier in these Reasons. I repeat paragraph 42 of these Reasons:

*[42] Thus, the background to what the ‘653 patent describes as its invention can be summarized as follows:*

- *Omeprazole, including its salts, was a well known “blockbuster” drug useful in the treatment of gastric acid related conditions.*
- *It was known that omeprazole was racemic and comprised two enantiomers.*
- *At least two known successful attempts at separating omeprazole into its enantiomers had been published - the Elandsson article and DE ‘455.*
- *Both enantiomers were useful in treating gastric acid conditions.*

[127] The separation of omeprazole into its enantiomers was not an easy task. I have earlier in these reasons reviewed DE ‘455, which describes a method of separating omeprazole into “optically pure” enantiomers.

[128] The other piece of prior art relied upon by Apotex in arguing that claim 8 of the '653 patent is obvious is the Erlandsson article. This article was mentioned at page 1 of the '653 patent as describing the separation of the enantiomers of omeprazole "*in analytical scale*". No further comment is made. At page 2 line 8 the '653 patent describes its new invention as a method of separating the enantiomers "*in large scale*".

[129] The Erlandsson article, at page 317 (Record, page 1400) describes that omeprazole was separated into (+) and (-) enantiomers of 82% and 95.6% (ee) purity. That is, the enantiomer of claim 8 was obtained with a 95.6% (ee) purity.

[130] The technique used by Erlandsson is described at the same page with reference to Fig. 8 as a "recycling" technique. This technique is commented upon by Dr. Collicott at paragraphs 29 to 37 and 97 to 141 of his affidavit (Record, pages 5663 - 5665 and 5676 - 5763) and Dr. Heathcock at paragraphs 219 to 233 (Record, pages 5764 to 5770) as routine analytical work. They opined that recycling could be carried out any number of times to reach whatever purity, as a practical matter, was desired.

[131] Dr. Armstrong, for AstraZeneca, at paragraphs 199 to 206 of his affidavit (Record, pages 601 – 602) describes the Erlandsson process as inefficient and producing only low yields. Dr. Davies goes further at paragraphs 132 to 138 of his affidavit (Record, pages 800 – 801) to state further that, in his opinion, the Erlandsson system could not be optimized to increase the optical purity.

However, he provides no support for this opinion. I view the evidence of these two witnesses not as

saying that the purity level could never be reached but as saying that it could not be done efficiently on any kind of practical scale.

[132] There was no serious argument raised by AstraZeneca that a person could and would be sufficiently motivated to make a salt of the esomeprazole enantiomer (see e.g. Dr. Myerson's affidavit, paragraph 94; Record, pages 5868 – 5869).

[133] The evidence of Dr. Heathcock in cross-examination makes the point that purity of a product is dependent on the use to which it is put. In pharmaceuticals, one would be motivated to make as pure a product as possible. He said in answer to questions 380 - 381 and 388 – 389:

380            *Q.     The level of purity that you want for a compound depends on the use of that compound.*

*A.     The level of purity you want for a compound depends on the intended use of the compound? Do I agree with that?*

381            *Q.     Yes, as a general concept.*

*A.     Yeah, I think I can agree with that. I'm just trying to think of all the possible situations where one might apply that statement, and it seems like a generally reasonable statement. If you are going to made cement out of calcium carbonate, it probably is different than if you are going to use it as an inert ingredient in a pill, for example.*

...

388            *Q.     Let me ask you this, Dr. Heathcock: are you disagreeing with me that in the context of pharmaceuticals – and you know omeprazole is a pharmaceutical, correct?*

*A.     Yes.*

389            *Q.     Are you disagreeing with me that in the case of pharmaceuticals, a skilled person would be motivated to make a pharmaceutical as enantiomerically pure as possible?*

*A.     No, I don't disagree with that.*

[134] I am satisfied, on the evidence that, as of the claim date, May 1993, it was known that omeprazole could be separated into its enantiomers (+) and (-), that they would be useful, just as omeprazole was, in treating gastric problems and that they could be processed in salt form with a salt such as magnesium. A purity of 95.6% (ee) for esomeprazole had been reported as having been achieved by Erlandsson. I am satisfied that the technique of Erlandsson could have been used to increase that purity to 99.8% (ee) if desired. One could readily be motivated to create a purer esomeprazole than reported by Erlandsson, given that the product would be used as a pharmaceutical.

[135] It is not a question as to whether Erlandsson's process was efficient or could produce large quantities of the enantiomer; it is only whether, given Erlandsson, it was obvious that one could achieve an enantiomer with 99.8% purity however inefficiently.

[136] Obviousness was discussed by Rothstein J. at paragraphs 69 and 70 of *Sanofi*, supra:

**69** *If an "obvious to try" test is warranted, the following factors should be taken into consideration at the fourth step of the obviousness inquiry. As with anticipation, this list is not exhaustive. The factors will apply in accordance with the evidence in each case.*

*1. Is it more or less self-evident that what is being tried ought to work? Are there a finite number of identified predictable solutions known to persons skilled in the art?*

*2. What is the extent, nature and amount of effort required to achieve the invention? Are routine trials carried out or is the experimentation prolonged and arduous, such that the trials would not be considered routine?*

*3. Is there a motive provided in the prior art to find the solution the patent addresses?*

*70 Another important factor may arise from considering the actual course of conduct which culminated in the making of the invention. It is true that obviousness is largely concerned with how a skilled worker would have acted in the light of the prior art. But this is no reason to exclude evidence of the history of the invention, particularly where the knowledge of those involved in finding the invention is no lower than what would be expected of the skilled person.*

[137] There was the means and motivation to make an enantiomer of high purity such as 99.8%.

This satisfies the requirements for obviousness. I find that Apotex's allegation that claim 8 of the

'653 patent is obvious, is justified.

#### CONCLUSION AND COSTS

[138] In conclusion, I find that Apotex's allegation that claim 8 of its '653 patent is invalid for lack of sound prediction and to utility as for obviousness, is justified. The allegation as to anticipation is not justified. The application is, therefore, dismissed.

[139] As to costs, Counsel agreed that they should be awarded to the successful party at the Column 4 level. They shall work out an appropriate quantum within a reasonable time, failing which they may apply to me for directions.

[140] No costs will be awarded for or against the Minister, who did not actively participate in these proceedings.

“Roger T. Hughes”

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Judge

**FEDERAL COURT**  
**SOLICITORS OF RECORD**

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**APPEARANCES:**

Mr. Gunars A. Gaikis FOR THE APPLICANTS  
Ms. Yoon Kang  
Ms. Tracey Stott

Mr. Andrew Brodtkin FOR THE RESPONDENT, APOTEX INC.  
Mr. Richard Naiberg

No One FOR THE RESPONDENT, MINISTER OF  
HEALTH

**SOLICITORS OF RECORD:**

Smart & Biggar FOR THE APPLICANTS  
Barristers & Solicitors  
Toronto, Ontario

Goodman LLP FOR THE RESPONDENT, APOTEX INC.  
Barristers & Solicitors  
Toronto, Ontario

Myles J. Kirvan FOR THE RESPONDENT, MINISTER OF  
HEALTH  
Deputy Attorney General of Canada  
Toronto, Ontario