Federal Court  Cour fédérale

Date: 20141118

Docket: T-1930-98

Citation: 2014 FC 1087

BETWEEN:

APOTEX INC.

Plaintiff

And

HER MAJESTY THE QUEEN

Defendant

REASONS FOR JUDGMENT

HUGHES J.

[1] Apotex filed a submission with Health Canada on January 25, 1988 for approval to sell a generic version of a trazodone (sometimes called trazadone) drug in Canada. Seven years later, after much correspondence, telephone conversations, meetings, the institution of two lawsuits – including one resulting in a decision by this Court – and a settlement agreement, Apotex received that approval in February 28, 1995. By that time, two generic competitors had already received approval to sell their versions of that drug in Canada.

[2] In October 1998, Apotex commenced this action for damages, including punitive damages, based upon multiple causes of action, including negligence, breach of a settlement agreement, misfeasance in public office, and misrepresentation, whether negligent, fraudulent or innocent. The Defendant, Her Majesty the Queen, has vigorously defended this action, including asserting that the claims are barred by limitation periods and statute; that Apotex has repudiated the settlement; that there was no duty of care owed and that Apotex did not mitigate its damages.

[3] For the reasons that follow, I find that Apotex is entitled in tort to damages but was required to mitigate those damages. The extent of those damages will be assessed at a later trial.

[4] The following is an index, by paragraph number, to these Reasons:

The Parties

[5] The Plaintiff Apotex Inc. is an Ontario corporation, having its head office in the City of Toronto. Apotex carries on business principally as a manufacturer of generic prescription pharmaceutical products for sale in Canada and elsewhere.

[6] The Defendant Her Majesty the Queen represents the Minister of Health and officials of the Ministry within the Health Protection Branch (HPB), responsible for examining pharmaceutical products before they are permitted to be sold or distributed in Canada for the purposes of determining safety and efficacy of those products, all as more particularly provided for in the *Food and Drugs Act*, RSC 1985, c. F-27 (FDA) and *Food and Drug Regulations,* CRC, c. 870, under that *Act*. Throughout the period of time relevant to this action, essentially 1988 to 1995, the HPB was organized and re-organized within a Drug Directorate (DD) and various Divisions and Bureaus of that Directorate.

The Evidence

[7] I commend Counsel for each of the parties for their co-operation in organizing the evidence and presenting it in an efficient manner. They agreed upon a large number of documents, which were produced in evidence without requiring formal proof of each and every one. Exhibit 1, which comprised four large volumes of documents – each identified with a numbered tab – were admitted into evidence by agreement, the full extent of which agreement is set out in Exhibit 4, but essentially provides that these documents will be received in evidence as being sent or authorized by the persons indicated on their face and received by persons so

indicated on or about the date apparent from the document. The truth of the contents was not admitted. A further single document, Exhibit 8, was admitted in evidence under the same terms.

[8] Also provided were books containing certain documents filed with the court in Judicial Review proceedings instituted by Apotex in this Court, T-2276-90 (Exhibit 2) and T-1877-91 (Exhibit 3).

[9] Certain facts admitted by the parties for purposes of this action were set out in Exhibit 5.

[10] The parties each submitted a booklet containing excerpts from the examination for discovery of the opposite party, which were deemed to have been read into evidence. The excerpts of the examination of the Defendant are found in Exhibits 14 and 21; and that of the Plaintiff in Exhibit 16.

[11] The Plaintiff Apotex called one fact witness and one expert witness in chief both of whom were examined and cross-examined. No witness was called in reply. Called were:

- Dr. Bernard Sherman, Toronto, Ontario, as a fact witness. He founded Apotex in 1977 and has been the controlling mind of that corporation ever since whether as President or as Chairman. He was personally involved in most of the events pertinent to this case from the Apotex side of things.

- Dr. Arthur H. Kibbe, Clarks Summit, Pennsylvania, as an expert witness. His qualifications are set out in an agreed statement provided on behalf of Counsel for each of the parties and marked as Exhibit 11. It says:

> *Expert in pharmaceuticals (pharmaceutical dosage form design, development and manufacture), pharmacokinetics, pharmaceutical excipients, the evaluation of the physical and chemical composition and therapeutic equivalence of formulations.*

[12] The Defendant, Her Majesty, called six fact witnesses and one expert witness. Called as fact witnesses, all of whom were examined and, except for Dr. Simon, cross-examined, were:

- Dr. Craig Simon, Ottawa, Ontario. Associate Director, Bureau of Pharmaceutical Studies. He did not join the organization until after 1995 and could only provide general information as to the period in question, 1988 to 1995. He was the person offered by the Defendant for discovery.

- Mike Ward, Ottawa, Ontario. Manager, International Programs, International Programs Division, Bureau of Policy, Science and International Programs Canada.

- Bruce Rowsell, Russell, Ontario. Retired, Former Director, Bureau of Pharmaceutical Surveillance.

- Dann Michols, Elgin, Ontario. Retired, Former Executive Director, Drugs Directorate and Former Assistant Deputy Minister, Health Canada.

- Mary Carman, Ottawa, Ontario. Retired, Former Director, Bureau of Nonprescription Drugs. During part of the relevant period, she was Mary Carman Kasparek.

- Dr. Wayne Nitchuk, Ottawa, Ontario. Retired, Former Acting Chief, Division of Biopharmaceuticals Evaluation, Bureau of Pharmaceutical Surveillance.

[13] Called as an expert witness for the Defendant was:

- Dr. Isadore Kanfer, Toronto, Ontario. Emeritus Dean and Professor, Faculty of Pharmacy, Rhodes University, South Africa. He was examined and cross-examined. His qualifications are set out in an agreed statement provided on behalf of Counsel for each of the parties and marked as Exhibit 17:

  > *Dr. Kanfer is an expert in the bioavailability and bioequivalence of drug products, including the scientifically valid methods for demonstrating bioavailability and bioequivalence, and the design, methods, Use (or application) of comparative dissolution studies in demonstrating bioavailability and bioequivalence. He is also an expert in biopharmaceutics.*

Obtaining Drug Approval in Canada - 1988 to 1995

[14] In the period from 1988 to 1995 and up to today, approval from the Minister of Health was and is required before a drug could be sold or distributed in Canada. That approval took the form of a Notice of Compliance (NOC) issued by the Minister. The Minister's officials were required to abide by the terms of the *Food and Drug* Act and *Regulations*, supra. In addition, the Minister periodically published Guidelines and policy statements which did not have the force of law, but were intended to provide guidance to those seeking approval, and the Minister's officials.

[15] In the present case, we are dealing with the period from 1988 to 1995. In late 1995, substantial amendments were introduced, which affect current practice, but not the practice during the relevant time period.

[16] The overriding concern of the Minister is that drugs provided to Canadians should be safe and effective for the intended purpose. A party seeking approval for a drug not previously sold in Canada - often called an innovator - is required to provide sufficient information, usually including extensive clinical studies, to satisfy the Minister as to safety and efficacy of that drug for the stated purpose. This is expensive and time consuming.

[17] A second party – often called a generic – who wished to sell or distribute that drug in Canada, could avoid the provision of clinical studies, provided that it could demonstrate to the Minister's satisfaction that its drug was sufficiently similar (and I use those words advisedly, because words such as identical and equivalent are important in this case) pharmaceutically and by way of bioavailability, so as to be a satisfactory substitute for the innovator's drug.

[18] I adopt and accept certain of the definitions given by the Defendant's expert, Dr. Kanfer, in his Report, Exhibit 18, in this regard:

> *Bioavailability*
>
> *Bioavailability refers to the rate and extent to which the API (active pharmaceutical ingredient)t, or its AM (therapeutic active entity) (substance), is absorbed from a pharmaceutical produce (dosage form) and becomes available at the site of action or biological fluids (plasma, serum or blood), representing the site.*

Bioequivalence

Two pharmaceutical (medicinal) products are bioequivalent if they are pharmaceutically equivalent and if their bioavailabilities in terms of the peak drug concentration in blood, serum or plasma (C_{max}) and time to reach the peak (T_{max}) and extent of absorption or total exposure expressed as the area under the drug concentration versus time profile (AUC) after administration of the same molar dose under the same conditions are similar to such a degree that their effects with respect to safety and efficacy can be expected to be essentially the same. The U.S.A's definition is:

> *...the absence of a significant difference in the rate and extent to which the active ingredient becomes available at the site of action when administered at the same molar dose under similar conditions in an appropriately designed study.*

Pharmaceutical equivalent

Pharmaceutical products are pharmaceutically equivalent if they contain the same amount of the same API (active pharmaceutical ingredient) in the same dosage form, if they meet the same or comparable standards, and if they are intended to be administered by the same route.

It is important to note that pharmaceutical equivalence does not necessarily imply bioequivalence as differences in the excipients (inactive ingredients Used as formulation adjuncts) and/or the manufacturing process can lead to changes in drug release and/or absorption.

The U.S.A FDA's definition is:

> *...drug products that contain the identical amounts of the identical active drug ingredient in identical dosage forms, but not necessarily containing the same inactive ingredients, and that meet the identical compendia or other applicable standard of identity, strength, quality, and purity, including potency and where applicable, content uniformity, disintegration times and/or dissolution rates.*

Therapeutic equivalence

Two pharmaceutical products are therapeutically equivalent if they are pharmaceutical equivalents and, if they can be expected to have the same clinical effect and safety profile when administered

> *to patients under the conditions specified in the labelling. Pharmaceutically equivalent products that are bioequivalent can be substituted for each other with the full expectation that the substituted product will produce equivalent clinical effects and safety profile as the original product.*

[19] The history of the use of bioequivalence by a generic as a substitute for clinical studies was discussed by Dr. Kanfer at paragraphs 15 and 16 of his Report:

> *15. Generic medicines contain the same active pharmaceutical ingredient(s) (API) as the innovator product, where previously the innovator has shown their prescribable product to be safe and efficacious based on clinical data from their initial clinical studies in humans. During the '70s the U.S. FDA decided that it was unnecessary for pharmaceutical companies seeking approval for generic products which contained identical active ingredients previously approved as safe and effective by the innovator companies to duplicate those initial clinical safety and efficacy studies. However, in lieu of those clinical studies in patients, a surrogate method known as comparative bioavailability (BA) or Bioequivalence (BE) studies comparing the genetic (TEST or "T") product with the approved product of original research (REFERENCE or "R") was introduced. This method focuses on the process by which the active ingredient is released from a dosage form and move(s) to the site of action.*
>
> *16. Such surrogate measures are justified by the presumption that concentrations of drug in the blood stream reflect concentrations at site(s) of action and that a relationship between the resulting systemic drug concentrations and the safety and efficacy of the drug is implied. Such studies circumvent the need to re-do time-consuming and costly studies in patients and involve an indirect measure of safety and efficacy where the concentration of the API in the blood of healthy human volunteers is measured following administration of the T and R products, each on different occasions in the same healthy human subjects. In other words, each subject receives both the T and the R product on different occasions and blood samples are collected at various intervals of time and analysed for the API. The resulting data are then Used to generate drug concentration profiles where the concentrations of drug are plotted versus time and the profiles resulting from the T and R are compared and assessed for equivalence, i.e. BE. The figure below is an example of a typical profile and associated parameters which are used to assess BE.*

[20] On occasion, a generic would offer evidence as to the dissolution rates of its drug as evidence of or in support of other evidence as to bioequivalence. A tablet would be dissolved in a liquid such as water, at different pH levels – and the dissolution over certain periods of time would be measured and often plotted on a graph. The drug at issue here was described as quick-dissolving, as it would be 95% dissolved within 15 minutes in water or 0.1 pH water solution. The acceptance of dissolution data in the circumstances of the present case was controversial.

Usual Practices of Health Canada – 1988 to 1995

[21] The Health Protection Branch (HPB) is the name generally used in these proceedings to indicate that branch of the Ministry of Health responsible for receiving and reviewing applications for a Notice of Compliance and issuing that Notice if the application were to be approved.

[22] Evidence was given by Dr. Simon and other witnesses for the Defendant as to the general practices followed by HPB in this process in the period from 1988 to 1995. An application would be received and given a brief review to ensure that the requisite documents, fees and so forth were provided. If that proved to be the case, a filing date would be assigned. Submissions would be examined in the order as received. There was a substantial backlog and significant delays in processing applications.

[23] If a file was examined and, if not found to be unsatisfactory, a letter would be sent to the applicant pointing out deficiencies, requesting further information, and so forth. The file would be put away and not looked at again until HPB received all the information requested and all

deficiencies addressed. Only then would the file be looked at again and only in sequence having regard to other files requiring examination. It was a tedious practice. It appears that the quickest that a generic could expect approval and an NOC was one to two years from the date of original filing.

Innovator Filings

[24] An innovator drug company, a name used to describe the company first to seek approval from HPB to sell a drug in Canada, was usually required to file data, including not only pharmaceutical information as to its drug; but *in vitro* (in glass – laboratory) testing, and *in vivo* (rats, etc) testing, and clinical testing on humans, of its drug. Where the drug was obtained from a manufacturer outside Canada who had already obtained approval from the country of manufacture, such as the United States, where there were rigorous drug approval studies conducted, HPB would accept data as submitted; for example, to the United States Food and Drug Administration, in respect of that drug.

[25] It was a policy of HPB not to look at the data submitted by the innovator for purposes of evaluating a submission by a generic who subsequently sought approval for the same drug. The generic could "reference" that data in the sense that approval had already been given by HPB, but HPB would not actually look at the data itself in the course of evaluating the generic's application. This policy does not appear to have a basis in law, as there is no provision in the *Food and Drug Act* or *Regulations* dealing with this matter.

Generic Filings

[26] It was a usual practice in the 1988 to 1995 period for a generic to test its product as against the innovator's product as approved in Canada for bioavailability (i.e. blood sampling over intervals). However, this was not an invariable practice. As the Agreed Facts (Exhibit 5) state, and the evidence of Dr. Sherman and several of the fact witnesses of the Defendants shows, there were at least a few instances where a product that had been approved for sale and sold in another country, such as the United States, was accepted during the period at issue as a reference product instead of a Canadian product. No clear or consistent reason for accepting a foreign reference product is apparent.

[27] The "policy" of Health Canada in respect of the use of a Canadian or foreign drug product as the reference product has a murky history.

[28] Guidelines dated February, 1981 (Exhibit 1, Tab 2) published by the Health Protection Branch, state at page 4, only:

> *...the bioavailability of the new generic drug product is compared to that of an acceptable standard...*

No definition of an *"acceptable standard"* was provided.

[29] It appears that in the 1980's, there was some general understanding, at least within HPB, that a Canadian reference product was required. This understanding was not reduced to writing

until a Memorandum was created by the Director General, Dr. Somers, on June 23, 1989 (Exhibit 1, Tab 28), which stated:

> *STANDARD FOR COMPARATIVE BIOAVAILABILITY AND COMPARATIVE PHARMACEUTICAL STUDIES*
>
> *In conformity with past Directorate practices, I wish to reiterate that New Drug Submissions (NDS) for 'generic' or synonym drug products should contain appropriate, adequate and validated data on comparative bioavailability studies.*
>
> *Such comparative studies should be performed by the use of the corresponding currently marketed Canadian drug formulation as the essential reference standard.*

[30] It appears that this Memorandum was never released to the general public although Apotex was given a copy on November 30, 1988.

[31] Some time in 1992, HPB published a *"Guidance for Industry"* concerning the Conduct and Analysis of Bioavailability and Bioequivalence Studies (Exhibit 10). It is a 49 page document which provides, at page 15:

> ***5.3 Selection of Reference Product***
>
> *For a new drug substance (i.e., the first market entry), an oral solution should be used as the reference product when possible. The oral solution can be prepared from an intravenous solution, if available.*
>
> *In bioequivalence studies, the reference product is:*
>
> *A drug product that has been issued a notice of compliance pursuant to section C.08.004 of the Food and Drug Regulations, and is currently marketed in Canada by the innovator, or*
>
> *a drug product acceptable to the Director.*

[32] There is no guidance as to what might constitute "*a drug product acceptable to the Director*".

[33] It must be made clear that neither the "policy" nor the "Guidance" respecting a suitable reference product is to be found in the *Food and Drug Act or Regulations*.

Apotex's Submission for an NOC – If A = B, and B = C, it follows that A = C

[34] On January 25, 1988, HPB received a submission from Apotex for a Notice of Compliance for a drug it called Apo-Trazad (later called Apo-Trazadone), in both 50 mg and 100 mg tablet form. It was a generic form of tablets containing the drug trazodone as the active ingredient.

[35] Apotex stated that its products would be manufactured in the United States by a company owned by it; Barr Laboratories. Apotex stated that Barr had obtained approval from the relevant United States authorities to sell its drug in the United States by providing data comparing the Barr drug to a drug called Desyrel, approved for sale and sold in the United States by an innovator company, Mead Johnson. Apotex provided a letter dated December 22, 1987, from Bristol the Canadian company who had received approval to sell the Desyrel product in Canada from Health Canada, Bristol, to a Canadian doctor, Dr. Rein. The letter said that the Canadian and United States Desyrel products were identical. In other words, in respect of a reference product, Apotex submitted that it would be selling the Barr product in Canada, that the United States authorities had approved the Barr product using the United States Desyrel product as a reference and, given that the Canadian and Untied States Desyrel products were identical,

Apotex should be permitted to use the same bioavailability studies relied upon by Barr in its United States application in Apotex's Canadian application.

[36] Some seven years later, after voluminous correspondence, many meetings and telephone calls, two judicial reviews having been instituted and one of them decided by this Court, and a purported settlement along the way, Apotex got its Notice of Compliance on February 28, 1995. The parties have admitted that two of Apotex's competitors, Pharmascience and Novopharm, had received Notices of Compliance for their generic trazodone tablets before Apotex did.

[37] It is useful to tabulate some of the more relevant documents and events provided in evidence. I attach this as Schedule A.

Apotex Files its Submission – Battle Lines are Drawn

[38] Apotex's submission for a Notice of Compliance for its Apo-Trazad 50 mg and 100 mg tablets was received by HPB on January 25, 1988 and received a preliminary screen. By letter dated April 25, 1988, HPB advised Apotex that the material would be reviewed "as soon as possible".

[39] The next substantive matter occurring within HPB was at a high level when the Director of the Bureau of Human Prescription Drugs, Dr. Johnson, sent a memorandum to the Director General of the Drugs Directorate, Dr. Somers, which clearly draws the lines that have been followed throughout the history of this matter: namely, on the basis of science alone, Apotex's

submission makes sense; the decision to be made is one of policy. It is worthwhile repeating this memorandum received January 30, 1989 (Exhibit 1, Tab 21):

> *NEW DRUG SUBMISSION FOR APO-TRAZAD – APOTEX INC.*
>
> *Apotex filed a New Drug Submission for Apo-Trazad on January 25, 1988, for the purpose of obtaining clearance for marketing the first generic Trazodone product.*
>
> *Trazodone is an antidepressant drug marketed for a number of years in this country by Bristol Labs.*
>
> *As you are aware, generic manufacturers usually supply bioavailability data as evidence of the safety and efficacy off their product. In this particular situation, Apotex would be expected to provide in their submission evidence of the bioequivalence of their product as compared with that of the innovator's brand marketed in Canada under the trade name of Desyrel. A preliminary review of the Apotex Submission, indicates that they have provided instead the results of a bioavailability study comparing the Trazodone product manufactured by Barr Laboratories in the U.S., with the standard innovator's brand manufactured in the United States by Mead Johnson. The comparative bioavailability study was carried out in Canada by BioResearch (Montreal) under a Canadian cleared IND.*
>
> *Since Barr Laboratories are owned by Apotex, they can presumably provide evidence that the Barr product and the proposed Apotex product are identical from a chemistry and manufacturing standpoint. Furthermore, they have obtained a letter from Mr. Leo P. Fleming, Manager, Technical Services, Bristol Laboratories of Canada to Dr. A. Rein in Toronto indicating that the product Desyrel sold by Mead Johnson in the United States is identical to the same product sold by Bristol in Canada. Therefore, it is not illogical to conclude that the bioavailability study done on the Barr and Mead Johnson products is applicable to the Apotex and Bristol products marketed in Canada.*
>
> *This point is further strengthened by the fact that the Mead Johnson product, in addition to being identical to the Bristol product, was in fact the product mainly used in carrying out pivotal studies performed in the U.S., which were also submitted in support of the Canadian NDS for Desyrel.*

> *Therefore, on the basis of science alone, I am inclined to accept the arguments advanced by Apotex. However, we should also examine the possibility that we may be establishing a precedent if we follow this course of action that could see us forced to accept similar arguments from around the world. What is to prevent, for example, Apotex from commissioning a bioavailability study comparing the French brand of a product as the standard? If we accept the arguments advanced in this particular case, we could have a difficult time not allowing this type of study. This could be the start of a process that would see us lose control over the generic submissions.*
>
> *Before a decision is made in this particular case I suggest that you contact Mr. L.B. Rowsell. In the future, his Bureau will be responsible for generic submissions and I do not want to take an action that might compromise his ability to carry out the duties that have been assigned to him. Perhaps when you have considered this memo you might wish to discuss it with Mr. Rowsell and give me your views on the issue.*

[40] Mr. Rowsell had, in 1988, assumed the role of Director of Bureau Pharmaceutical Surveillance within the Drug Directorate. His job was to oversee the people who did the actual evaluation of submissions for drug approval. He had an undergraduate degree in pharmacy. He did not do any of the actual reviewing or evaluating himself.

[41] The matter was apparently referred to Mr. Rowsell because on February 8, 1988, he wrote a memorandum to Dr. Somers (Exhibit 1, Tab 22) stating that he anticipated substantial difficulty in establishing that the United States reference product was identical to the Canadian product and that this *"emphasizes the need for clear guidelines to express our requirements"*.

[42] There followed the internal policy statement of Dr. Somers of June 23, 1989, previously referred to, as well as internal memoranda involving Ms. Mary Carman (Kasparek) and correspondence with Apotex (Dr. Sherman) as to the propriety in using a non-Canadian drug as

the reference standard. Dr. Johnson provided his view to Ms. Carman in a memorandum dated July 10, 1989 (Exhibit 1, Tab 30):

> *STANDARD FOR COMPARATIVE BIOAVAILABILITY AND COMPARATIVE PHARMACEUTICAL STUDIES*
>
> *I am in receipt of your memo of June 30th on this topic together with the correspondence dated June 29th and April 3rd from Dr. Sherman. I would like to make the following comments:*
>
> *1. I believe that we should accept data comparing the generic product against the innovator's brand as sold in a major market of the world if we have evidence that the innovator does not have manufacturing capabilities in Canada and must import his product from the major market country.*
>
> *2. I do not believe we should accept studies conducted outside Canada against the innovator's brand as sold in a major market area if the innovator has manufacturing capabilities in Canada and formulates his product in our country. Although the innovator's product may have the same master formulation throughout the world, differences in equipment and personnel may affect the overall performance of a product and we have no guarantee that the product manufactured by Merck, for example, in the United States is identical to a product bearing the same name and manufactured by the same company in Canada.*
>
> *3. It is correct that in many cases the originator has obtained his Canadian Notice of Compliance on the basis of data generated on a product sold in a major market, however, in the subsequent years it is the Canadian formulated product that has been accepted as being safe and efficacious in Canada on the basis of its track record in large numbers of Canadian patients. It must, therefore, remain our "gold standard" against which imitators should make their comparisons.*

[43] On June 29, 1989 (Exhibit 1, Tab 29) Dr. Sherman wrote to Dr. Somers, re-iterating his position that a United States reference product was appropriate. In response, Dr. Somers wrote to Dr. Sherman on August 24, 1989,(Exhibit 1, Tab 32) rejecting this proposal, saying:

> *In your letter of June 29th, you proposed that if a series of conditions were met in their entirety, the Health Protection*

Branch could forego its normal requirement for Canadian sourcing of the reference dosage form.

The requirement for Canadian sourcing allows a manufacturer to establish, in very exact terms, that their test product releases drug into the systemic circulation at the same rate and extent as does the reference dosage form. Where the safety and efficacy profile of the reference drug product is acceptable, this offers a scientific basis to assert that, apart from possible effects from impurities or excipients unique to the dosage form, the test product will also be acceptably safe and effective. The basis for the acceptability of the Canadian reference product stems from both premarket data on file with the Branch and the subsequent years of performance by the product in Canada. This aspect of performance is greatest for the first brand of that drug product to enter the Canadian market and therefore is the appropriate norm for comparison.

When the reference product cannot be conclusively proven to be identical to that marketed in Canada, parity of performance with a product known to the Branch can not be assumed.

The alternative is for the manufacturer of the test product to abandon comparative bioavailability studies with marketed products and conduct original clinical research to establish the safety and efficacy of the test product.

The conditions that you have proposed to forego Canadian sourcing of the reference product do not conclusively prove that a non-Canadian reference product is identical to the Canadian version. Additionally two of the conditions bear special note.

With respect to your condition 4., the Branch is not at liberty to consult the file of another manufacturer to determine the extent to which their data was generated using a product formulation that was sold in a different country. As well, subsequent Branch experience will have been with the formulation marketed in Canada and the Branch need not have been apprised of ensuing formulation changes made to the product in another country.

> *Secondly, stipulation to intend to sell the product in other countries, as noted in your condition 6., does not temper the mandate of the Food and Drugs Act for Canada.*
>
> *I trust that the preceding explanations clarify the Branch position on Canadian sourcing of the reference dosage form for comparative bioavailability studies.*

[44] It was clear by this time that the battle lines had been drawn. Apotex wanted to use a United States reference standard; HPB insisted on a Canadian standard, unless the United States reference product could be *"conclusively proven to be identical"* to the Canadian product. The evidence before me is that it is almost impossible to demonstrate that any drug product is "identical" to another, even tablets taken from the same batch (e.g. Dr. Kibbe's Report, Exhibit 12, para 38). Some measure of difference must be tolerated.

[45] Apotex continued to press; HPB "reanalyzed" the data it had received from Apotex. A Mr. Michalko, Chief, Division of Biopharmaceutics Evaluation, came into the picture. On November 30, 1989 (Exhibit 1, Tab 38) he wrote to Apotex a peculiar letter attempting to bootstrap HPB's insistence on a Canadian reference product by reliance upon HPB's unpublished policy that had been reduced to writing after Apotex had filed its submission. On December 18, 1989, Michalko wrote to a Mr. Jeffs, Assistant Director-Operations, Bureau of Human Prescription Drugs (Exhibit 1, Tab 39) asking whether the "policy" that HPB had respecting its refusal to look at third party information to gain information in order to verify if the submission – in this case, of Apotex – was correct. On February 1, 1990, Michalko wrote to Apotex stating that HPB would not look at another party's submission.

[46] Here I pause to repeat what Apotex's Counsel stated in argument before me. HPB already knew that the United States reference product relied upon by Apotex was identical to the Canadian drug sold by the innovator. They knew this because, in approving the innovator's drug for sale in Canada, the innovator had provided the data from its United States product. If HPB had referred to the innovator's file, it would know that the United States product was identical to the innovator's Canadian product. By refusing to look at this file, HPB was requiring Apotex to prove to HPB that which HPB already knew to be true. The only reason for refusing to look at the other file was "policy".

[47] In late 1989, and until August 1990, when Apotex filed its first Originating Motion for Judicial Review, there was an exchange of correspondence between Apotex and HPB. I will not recite all of this; suffice it to say that each party stuck to its position as to whether a Canadian reference product was required and whether a United States reference product could be used.

[48] Apotex filed an application for judicial review with this Court in August, 1990.

Judicial Review # 1: T-2276-90

[49] On or about August 13, 1990, Apotex filed an originating Notice of Motion (as was the practice then) with the Court seeking an Order directing that the Minister review Apotex's Apo-Trazad applications without requiring that the reference product be purchased in Canada, and to issue a Notice of Compliance to Apotex. Court file number T-2276-90 was assigned to the matter. The pertinent requests were for an Order:

> *(a) Directing the Respondent Minister of National Health and Welfare (the "Minister") to review the Applicant's New Drug submission in respect of its drug product, Apo-Trazad, to determine whether same, and more particularly, the comparative bioavailability study, literature review and other data contained therein, adequately establish the safety and effectiveness of Apo-Trazad for use as a drug in Canada without regard to a condition precedent to such review that the reference product tested in the comparative bioavailability study be purchased in Canada;*
>
> *(b) Directing the Respondent Minister, upon completion of the review of the Apo-Trazad New Drug submission, if such review is satisfactory, to issue a Notice of. Compliance in respect thereof;*

[50] Apotex discontinued that proceeding upon a settlement having been reached with the Minister.

Settlement Agreement

[51] On November 5, 1990, Apotex, represented by Dr Sherman, and its lawyer Harry Radomski, met with Bruce Rowsell, representing the Minister and Marlene Thomas, a Department of Justice lawyer representing the Minister in order to settle the litigation in T-2276-90. The result was a letter from Ms. Thomas to Mr. Radomski dated November 26, 1990. This letter is referred to as the Settlement Agreement and said:

> *This letter confirms the agreement reached between the parties and counsel as to the settlement of this action, culminating in its withdrawal without costs before Jerome, A.C.J. in Motions Court of the Federal Court, Trial Division in Toronto on November 19, 1990.*
>
> *The Respondents hereby provide the following statement with respect to the subject matter of the litigation:*
>
> > *Further to recent discussions, this confirms that the review of your Apo-trazad new drug submission is continuing and has not been completed for the*

> *purposes of section C.08.004 of the Food and Drug Regulations. If there are any deficiencies, they will be identified upon completion of the examination.*
>
> *Any existing and further data provided by Apotex to establish that Apo-trazad is chemically and therapeutically equivalent to a drug product sold in Canada will be considered. For the purposes of a comparative bioavailability study, the Health Protection Branch is prepared to consider evidence to establish equivalency between Canadian and non-Canadian reference standards.*

I believe this concludes the matter.

[52] Ensuing matters did not proceed well.

Ensuing Matters-Not All is Well

[53] Things did not go well after the Settlement Agreement letter was signed by Ms. Thomas and given to Apotex. In his reasons given in the second judicial review, which I will discuss in some detail shortly, Justice MacKay set out at considerable length what went on within HPB and between HPB and Apotex. I refer in particular to paragraphs 17 to 30 and 38 to 87 of his reasons, reported at 59 FTR 85. Having heard the witnesses, and having reviewed the documents in evidence in the case before me, I endorse and confirm his findings.

[54] I accept Dr. Sherman's evidence as to the discussions leading up to the Settlement Agreement, and I reject Mr. Rowsell's evidence in that respect. It is clearly evident from the discussions between Apotex and HPB that the only outstanding issue was that of bioavailability. The parties were apart in that respect, in that Apotex believed that it could demonstrate bioavailability by equivalency, whereas HPB was looking at identicality. The Settlement

Agreement clearly states that HPB will look at the matters from the point of view of equivalency. To say that the Agreement was ambiguous or that HPB didn't know what the parameters were for equivalency is disingenuous. Sherman and Rowsell were at the settlement meeting; if HPB had any concerns respecting equivalency, they could have been raised then, and clarified then. HPB's lawyer wrote the Settlement Agreement letter; if she or her client had any doubts about what she was writing, they should have expressed them at the time. HPB knew what the letter meant.

[55] However, HPB did not follow the terms of the Settlement Agreement. It stayed on a path whereby they were insisting upon identicality. HPB was less than full and forthright in its dealings with Apotex. I find that there was a deliberate attempt by HPB to stick to its position as to identicality while conveying to Apotex a sense that it was willing to be flexible, which it was not.

[56] Apotex, correctly in my view, was led to believe that the submission to HPB of a bit more data; particularly with respect to dissolution, would be sufficient to satisfy HPB. It supplied such data. The uncontradicted evidence of Apotex's expert Dr. Kibbe (Exhibit 12, paras 38 to 65) is that this evidence should have been sufficient to satisfy HPB as to equivalency.

[57] Dr. Sherman, on behalf of Apotex, wrote to Dr. Somers of HPB a letter dated April 25, 1991 (Exhibit 1, Tab 83). It said, *inter alia*:

> *Your letter of March 8, 1991, reporting the results of review of our NDS, states under point 1 that there remains a requirement for a bioavailability study using a Canadian reference.*

Our submission was filed on January 25, 1988, over 3 years ago, and is one of the oldest uncleared submissions at HPB.

We received a letter from Dr. DaSilva dated May 1, 1989 stating that a Canadian reference was needed, and the matter has been under debate between Apotex and HPB since that time. It has been and remains our position that the reference need not be purchased in Canada; in fact, logically the preferred reference should be that to which the literature establishing safety and effectiveness most closely relates, that being the reference as sold in the originator's home market.

As you know, we brought an action in the Federal Court in August 1990, which was withdrawn only after we arrived at a settlement agreement. The agreement was that the U.S. reference could be used, along with evidence to establish the equivalence of the Canadian and U.S. references. In the course of settlement discussions, we provided Mr. Rowsell with IR spectral comparisons and dissolution comparisons, as further evidence that the formulations of the U.S. and Canadian references were the same, and he confirmed that this data was the type of further data needed.

In the course of settlement discussions, we received assurances that HPB would comply with the agreement and review our submission in good faith.

. . .

If Mr Rowsell did not know that there were other examples of use of a reference not purchased in Canada, then it can only be because he failed to inform himself, in which case he should not have sworn in paragraph 3 of his affidavit that: "I have knowledge of the matters herein stated".

Apotex is now suffering substantial damages from the delay in review and approval of Apo-Trazadone.

We ask that you reconsider your position and confirm that our bioavailability study using the reference purchased in the U.S. will suffice. If we do not receive such confirmation within a matter of days, we will have no alternative but to initiate another action in the Federal Court founded, inter alia, on bad faith and on refusal to comply with the settlement agreement. We will also claim damages flowing from the delay in review and approval.

Please reply promptly, as time is of the essence.

[58] On July 2, 1991, Dr. Sherman again wrote to Dr. Somers (Exhibit 1, Tab 102). This lengthy letter concluded:

> *In summary, we believe it clear that a policy that the reference must be purchased in Canada is not well-founded on several grounds. We believe HPB must abandon that position, or, or, in the alternative, comply in good faith with the Settlement Agreement, whereby the foreign reference may be used in cases in which the foreign and Canadian references appear to be the same and the lack of any significant difference is confirmed by laboratory comparisons.*
>
> *I urge you to carefully reconsider your position in light of the contents of this letter and to confirm that our studies are now acceptable in accordance with the Settlement Agreement.*
>
> *In the event that your answer remains negative, which I hope will not be the base (sic), we will have no alternative but to promptly proceed with further steps in the Federal Court. In view of the severe damages now accruing, we will not limit our action to an Application for an Order in the nature of mandamus, but we will also pursue a statement of claim for damages.*
>
> *I will phone you tomorrow to determine your answer.*

[59] Again, on July 31, 1991, Dr. Sherman wrote to Dr. Somers (Exhibit 1, Tab 111) a lengthy letter which concluded:

> *<u>Summary</u>*
>
> *I believe that each and every one of the "comments" made by you is untenable. Moreover, taken together they appear to demonstrate an intransigent refusal to act in good faith.*
>
> *Damages to Apotex are rapidly accruing, and I urge you again to immediately confirm the acceptability of our submissions, so as to avoid the need for us to pursue the Notice of Motion and a claim for damages.*

[60] Apotex filed its second judicial review application on July 17, 1991.

Judicial Review #2: T-1877-91

[61] On July 17, 1991, Apotex filed a second originating Notice of Motion with the Court, assigned file number T-1877-91. Apotex sought in respect of the Minister, the following Order:

> *(a) Directing the Respondent Minister of National Health and Welfare (the "Minister") to review the Applicant's New Drug Submissions in respect of its drug products, Apo-Trazad and Apo-Zidovudine, to determine whether same, and more particularly, the comparative bioavailability study, literature review and other data contained therein, adequately establish the safety and effectiveness of Apo-Trazad and Apo-Zidovudine for use as a drug in Canada without regard to a condition precedent to such review that the reference product tested in the comparative bioavailability study be purchased in Canada or that there be a certification from the manufacturer of the Canadian reference product that it is identical to the non-Canadian reference product;*
>
> *(b) Directing the Respondent Minister, upon completion of the review of the Apo-Trazad and Apo-Zidovudine New Drug Submissions, if such review is satisfactory, to issue a Notice of Compliance in respect thereof and if such review is unsatisfactory, to detail the deficiencies disclosed in such review;*

[62] Among other Affidavits, the Affidavits of Bernard Sherman and Bruce Rowsell were filed, both of whom were cross-examined. It must be noted that Apotex put in issue not only its Apo-Trazad submission, which is the subject of this action, but also another submission,one for Apo-Zidovudine in which Apotex had also used a non-Canadian reference product. In his reasons, to which I will now turn, the late Justice MacKay of this Court identified the Apo-Trazad application as Apo-A, and the Apo-Zidovudine application as Apo-B, as there were at that time certain concerns as to confidentiality.

[63] This application was heard by Justice MacKay on March 22 to 24, 1992. He delivered his decision, with reasons, on January 19, 1993. His reasons, as reported at 59 FTR 85, were put before me in the agreed evidence as part of Exhibit 3.

Apotex Mitigates on Apo-Zidovudine

[64] With respect to Apo-B (Apo-Zidovudine), subsequent to the hearing in March 1992, Apotex provided to HPB a bioavailability study using a Canadian originator product as a reference. Apotex was given a Notice of Compliance by the Minister on May 25, 1992. This matter was brought to the attention of Justice MacKay before he had given his decision. As a result, Justice MacKay dismissed Apotex's application respecting Apo-B as moot. His reasons in this respect are set out at paragraphs 31 to 37. I will not reproduce those reasons here.

[65] With respect to its Apo-Zidovudine application, Apotex wrote to Mr. Rowsell on May 10, 1991 (Exhibit 1, Tab 87) challenging the "policy" respecting the use of a Canadian reference product. The letter stated, in part:

> *If we do not receive your prompt confirmation that the U.S. reference is acceptable and review has commenced, we will instruct our solicitors to apply to the Federal Court for an appropriate order. We will also mitigate damages by commencing the repeat study and will seek to hold HPB liable, for both the cost of the study and damages from delay in review and approval.*

[66] In fact Apotex did conduct a study using a Canadian reference product and did receive approval for Apo-Zidovudine within a few months. When cross-examined on this point, Dr. Sherman provided the following answers at pages 474 to 477 of the Transcript:

Q. It was your – was that – was that a statement of a – a real intention to do so?

A. Yes. And I can tell you what happened. We were in a real hurry for this one because it was a first generic opportunity of a substantial significance, but in addition, what distinguished this product was that Health Canada had a fast-track policy for antiretroviral drugs.

So in this case we knew that if we did a repeat study and submitted it, it would not result in the long delay for – to put it back at the end of the line because the antiretrovirals immediately went to the front of the line so there would be no delay.

So as a pragmatic matter we recognized that doing the mitigation, doing the repeat study was the faster route because a judicial review would have taken a lot longer.

There'd be no delay other than the delay of doing the study which, in this case, was relatively quick. It was a simple study we could do in a couple of months. So pragmatically the best way to do it was to do a repeat study for that reason of fast tracking.

And at the end we didn't bother suing for damages because it just wasn't worth it. We really weren't delayed much because for the very reason that I told you.

And also Health Canada was, in any event, because of the fast-track policy already reviewing the submission, in any event, even while we were doing the repeat study and to sue for a couple hundred thousand dollars and the cost of the study would have made no sense.

That's what happened in this case.

Q. I thought apo-trazadone was an antidepressant?

A. It is. We're talking about AZT here, are we not? Yes, we're not talking about AZT, zidovudine. Yes, we're not talking about trazadone in this – in this letter. It was zidovudine, AZT.

Q. I apologize, but the letter –

A. You're dealing with zidovudine which is AZT. I guess AZT since we're in Canada.

Q. I see. So in this case you are advising Health Canada right from the start that if we can't get this going we're going to do a study –

A. Yes, for the reason –

Q. - and then come after you for damages?

A. The reason I told you, but then the – it turns out that there was no significant delay as a result and the only damage would be the cost of the study which is only a couple hundred thousand dollars. Wouldn't make sense to sue for that.

Q. And in this case, I believe you said it pragmatically was the best thing to do?

A. The suit, yes.

Q. No, to do the bio –

A. In the case of AZT –

Q. To sue, I'm sorry. Yes.

A. In this case, the case of apo-trazadone if we'd done the repeat study it would have taken time and then we would have gone back to the beginning of the queue. It would – that would have delayed us another year.

Back to Judicial Review #2: T-1877-91

[67] Justice MacKay dismissed the application with respect to Apo-A (Apo-Trazad). He did so having reviewed many of the facts and documents as put in evidence before me, including, what was done by HPB before and after the Settlement Agreement. Apotex's Counsel argues that Justice MacKay did not have the complete picture, since the matter was dealt with as an application where no discovery was available. Apotex's Counsel argues that, as a result of Access to Information requests and the discovery process in this action, a much more complete picture as to what went on at HPB is in evidence before this Court.

[68] Justice MacKay provided extensive reasons. At paragraphs 8 to 16, he sets out the general procedure in effect in the early 1990's for obtaining a Notice of Compliance. At paragraphs 17 to 30, he reviewed, in general, Apotex's application for approval of Apo-A (Apo-Trazad). He then dealt with the Apo-B Apo-Zidovudine) application, which I referred to earlier. He returned to the Apo-A application at paragraphs 38 to 87. I repeat paragraphs 85 to 88 of his Reasons, wherein he dismissed the application on the basis that the determinations of HPB were not "patently unreasonable":

> *In judicial review of specialized tribunals, such as labour relations boards or adjudicators whose decisions, based upon particular expertise and experience, are to be final and binding and not subject to appeal or review, it is now accepted that a court will intervene only where the decision maker has interpreted governing legislation in a manner that is so patently unreasonable that it demands intervention by the court. (Canadian Union of Public Employees, Local 963 v. New Brunswick Liquor Corp., [1979] 2 S.C.R. 227, 97 D.L.R. (3d) 417 per Dickson J. as he then was). In view of the discretion here, requiring special expertise and informed scientific judgment it seems to me a comparable sort of standard is appropriate for this Court to consider in this case. Put as a question, in view of the particular, specialized discretion here vested in HPB can it be said that its application of the governing regulation, section C. 08.002, to require evidence of a bioavailability study comparing Apo-A and C (Can.) in the new drug submission for Apo-A is patently unreasonable? Is it so unreasonable that the governing regulation clearly will not support its application in this way?*
>
> *Viewed against that standard, the evidence on behalf of the respondent Minister, particularly that of Dr. McGilveray, though disputed by Apotex, the fact that in many previous. submissions by Apotex itself bioavailability studies were included with reference to a Canadian standard product, and HPB's reference to practices followed in some other countries, lead me to conclude that there is no basis for this Court to determine that the HPB requirement is patently unreasonable or beyond the discretion of the Director under section C. 08.002 of the regulations.*
>
> *Except for the refusal to consider the bioavailability study comparing Apo-A with C (U.S.), the Minister's responsibility to consider the Apotex submission was met, ultimately by the letter of*

> *March 1991 advising that the new drug submission at that stage did not meet requirements for compliance with the regulations. Among other deficiencies then noted was the failure to establish the safety and efficacy of Apo-A in comparison to a Canadian reference standard, which Apotex concluded meant there was a requirement for a bioavailability study using a Canadian reference, a conclusion borne out in subsequent correspondence with HPB. That requirement for a revised new drug submission has not been met by Apotex. Until there is such a submission, no duty rests on the respondent Minister to again consider the issuance of a notice of compliance for Apo-A.*

[69] On February 8, 1993, Apotex appealed from the decision of Justice MacKay (A-135-93: Exhibit 3 Tab 20); further discussions between the parties occurred. The appeal was withdrawn once Apotex received its Notice of Compliance for Apo-Trazad (Apo-A) February 28, 1995.

Justice MacKay's Findings

[70] In the course of his Reasons, Justice MacKay made a number of findings. While there was an appeal taken by Apotex, it was ultimately withdrawn. Therefore, those findings are final. I appreciate that those findings were based on the record before Justice MacKay and the issues before him were in the context of a judicial review. I further appreciate that there is additional evidence before me, and that unlike Justice MacKay, I have seen witnesses in person. I pause to note that it is agreed by counsel for each of the parties that Justice MacKay's use of the word "discovery" in his Reasons is directed to transcripts of cross-examination of persons who had filed affidavits in the proceedings before him and not on a discovery.

[71] Having heard the witnesses before me, and having reviewed the evidence before me, I concur with a number of the findings made by Justice MacKay. This oral testimony of the

witnesses, and these further documents, serve to confirm his findings, which I adopt as my own. In particular, the following findings:

- Apotex understood that the Settlement Agreement required that equivalency between the U.S. reference brand used by it in its bioavailability study and the Canadian originator brand, by laboratory tests; in particular chemical analysis and dissolution studies, was what the Settlement Agreement contemplated. HPB said it was prepared to "consider" information and, through Counsel, HPB conceded that it was satisfied as to chemical equivalency. At paragraph 47 he wrote:

  > *Particularly after the settlement in 1990 of the first application for judicial review in relation to Apo-A, Apotex sought to establish equivalency, between the U.S. reference brand used for its bioavailability study and the Canadian originator brand, by laboratory tests, in particular chemical analysis and dissolution studies. That was what Apotex understood, as a result of the settlement agreement, would establish equivalency. That understanding apparently was not shared by HPB. Although HPB held out that, in accord with the settlement, it was prepared to consider any information Apotex submitted, and that it had done so, the submissions by Apotex did not satisfy HPB. At the hearing of this matter, counsel for the Minister conceded that HPB was satisfied with chemical equivalency of the two reference brands, but it was not satisfied that the test data submitted by Apotex established their therapeutic equivalence.*

- There was still controversy as to whether dissolution studies were sufficient so as to establish bioavailability. He wrote at paragraphs 49 and 51:

  > *As I interpret these comments, they stress the difference between dissolution studies and bioavailability studies, a difference Apotex would not deny, and they highlight, from HPB's perspective, the limitations of dissolution studies for purposes of establishing therapeutic effectiveness when contrasted with bioavailability studies comparing the drugs*

> *under study in their use with human subjects by in vivo tests.*
>
> . . .
>
> *In regard to these concerns Mr. Sherman, by affidavit in response, urged that HPB's concern with changes to drug products properly related to drugs marketed in Canada. In examination on their affidavits both Mr. Rowsell and Dr. McGilveray, spokespersons for HPB, ultimately concede that, at least in theory, dissolution studies could be designed to indicate any significant differences in formulation and manufacturing processes used for drugs compared in the studies. In fact, Mr. Rowsell professed no personal expertise in dissolution studies and deferred to Dr. McGilveray as an expert. The latter professed no personal knowledge of the Apotex studies and spoke to dissolution studies on the basis of general principles. He acknowledged that such studies were acceptable for purposes of comparing chemical and therapeutic equivalence in different batches of the same drug produced by one manufacturer, even, as I understand it, when produced in different factories. Yet he declined to accept Apotex dissolution studies as a basis for establishing therapeutic equivalence of C (Can.) and C (U.S.) even though, belatedly, chemical equivalency was accepted. Neither Mr. Rowsell nor Dr. McGilveray were knowledgeable about the details of any review by HPB of the Apotex studies, though they were put forward as spokespersons on behalf of HPB and the respondent Minister. It is apparent from their examination in discovery that their views reflected general considerations and circumstances rather than positions adopted after any personal consideration of the particulars of the Apotex submissions.*

- Despite its assertions to Apotex that HPB was prepared to accept evidence as to equivalency of the U.S. and Canadian products, in fact HPB was only prepared to consider evidence as to bioavailability with reference to a Canadian product. He wrote at paragraph 55:

  > *My own review of this portion of the evidence leads me to conclude that, in the final analysis, HPB refuses to accept, for purposes of establishing safety and effectiveness*

> *of the Apotex brands, evidence of equivalency of U.S. and Canadian originator products. The emphasis, in Rowsell's affidavit, on comparing manufacturing processes used in preparation of the Canadian and U.S. originator brands, which ordinarily would be beyond the ability of Apotex to obtain, in my view makes clear that HPB was not prepared to consider equivalency of the two originator brands on the basis of any evidence Apotex could produce by laboratory tests. Despite its protestations that it would consider, in relation to the Apo-A submission, any further information Apotex submitted, HPB was only prepared to consider as sufficient a bioavailability study with reference to the Canadian originator product, C (Can.). HPB clearly stated that no other method satisfactory to it for establishing equivalency had been identified. While formally HPB's position was open to consider Apotex submissions, for all practical purposes only the submission of a satisfactory bioavailability study of Apo-A and C (Can.) would satisfy HPB of the safety and effectiveness of Apo-A.*

- HPB was disingenuous in representing to Apotex that it was prepared to consider all other submissions. HPB remained adamant that only a Canadian reference product would suffice. He wrote at paragraph 56:

> *If those responsible for HPB knew at the time of the settlement with Apotex in 1990 that there was no method satisfactory to HPB identified to establish equivalency of the U.S. and Canadian reference brands, then, in my view, in the settlement HPB misrepresented that they were prepared to consider information to establish that equivalency. If it became clear only after the settlement that no other method could establish equivalency to HPB's satisfaction, it seems to me disingenuous to continue to say they were prepared to consider all other submissions of Apotex for this purpose, when in effect only the submission of a bioavailability study with reference to C (Can.) would suffice to establish safety and effectiveness in human use of Apo-A.*

- There is little evidence to support HPB's assertion that there was a "long-standing" policy requiring a Canadian reference product. He concluded at paragraphs 63 and 64:

I find it surprising that the evidence offered in support of the existence of a policy, said to be of long-standing, is all of such recent origin. Moreover, no explanation is offered of the interrelation of the policy, if it were of long-standing, with omission of any reference to it in ***Guidelines for New Drug Product Requirements*** *published in February 1981 by the then Bureau of Human Prescription Drugs of HPB. These guidelines include reference to "General Requirements for Safety and Efficacy" and to "Bioequivalence", and both references refer to studies relating to acceptable brands of the drug product under review. It is noted that drugs may be introduced in different countries. In relation to Bioequivalence the guidelines state that "Generally the bioavailability of the new generic drug product is compared to that of an acceptable standard, in studies in man using an ethically acceptable dose and a validated method". No reference is made to any necessity for studies to be related to a Canadian reference brand. Though these guidelines might be changed by HPB acting within discretion vested by regulation C. 08.002 (see, in relation to a change in regulatory policy regarding the definition of "new drug" under C. 08.001, C. E. Jamieson & Co. (Dominion) Ltd. et al. v. Canada (Attorney General) (1987), 12 F.T.R. 167 at 213, 46 D.L.R. (4th) 582 at 644, 37 C.C.C. (3d) 193 at 255), there is no evidence that the guidelines were revised and published, as the 1981 version was, for the guidance of the industry. If HPB policy was of long-standing, I find it extraordinary that Apotex, a major generic drug manufacturer, was unaware of it until the matter was brought to its attention by HPB in the latter part of 1989 in response to an Apotex new drug submission other than for Apo-A. In its timing, the communication of HPB's policy statement to Apotex was after its new drug submission for Apo-A, though Apotex apparently conceded it was aware of the policy before its new drug submission for Apo-B was put forward to HPB.*

My conclusion is that HPB may well have had a practice, not followed dogmatically as we shall soon see, which practice was reduced to writing, as a policy statement, in June 1989, that bioavailability studies submitted in relation to new generic drugs where an originator brand is already available in the Canadian market should be done with reference to the brand currently sold in the Canadian market. That is what the internal policy memorandum of June 23, 1989, clearly says. That may have implications for circumstances where

> *a generic brand is the first of a drug product to be brought to market in Canada, if those circumstances are possible, but those are not relevant here. The use of the verb form "should be" in the policy statement may be intended to be mandatory, but it evidently is intended as a directive for the future.*

- HPB was inconsistent in applying its "policy" with respect to insistence upon a Canadian reference product. However, there is no evidence that Apotex was subject to discrimination in this regard. He wrote at paragraph 67:

> *The record is one of less than consistency in the application of its stated policy or practice by HPB, though Apotex may well have been no worse off or no better off than any other manufacturer. The record does not depict an efficient, effective HPB in terms of its relations with Apotex, one of the manufacturers whose products it is required to approve for sale in Canada. Apotex was itself the beneficiary of decisions accepting studies with reference to foreign originator products in other cases. Nevertheless, it is difficult to agree that it was subject to discrimination or even unfairness from the requirement of HPB in this case on submission of a bioavailability study with reference to the Canadian product for the discretion of the Minister and his advisers is to be exercised in relation to each application and I am not persuaded there is a firm basis here for comparing applications for similarities in all relevant respects.*

- While the *Food and Drug Act* and its *Regulations* vest discretion upon the Minister, that discretion is not unlimited and must be exercised on consideration of the relevant factors set out therein. He wrote at paragraph 75:

> *In my view the regulations vest complete and exclusive discretion in the respondent Minister and the Director of HPB to determine the requirements of a new drug submission in terms of the information or evidence to be provided by the manufacturer. That discretion is not unlimited, for it must be exercised on consideration of factors that are relevant to the purposes of the Act and regulations. Those purposes, in relation to new drugs, are to provide a process for approval of new drugs to be marketed in Canada that is "in the interest of, or for the*

prevention of injury to, the health of the purchaser or consumer" (the Act s. 30(1)(e)).

- The refusal by HPB to consider Apotex's full submissions on the basis that a Canadian reference product was required was an unlawful fettering of its discretion. There was no lawful basis for refusing to do so. He wrote at paragraphs 78 and 80:

> *In my view, refusal to consider the full submission for Apo-A because of a claimed policy that bioavailability studies be done only with reference to a Canadian product, as for a time appears to have been the position of HPB following the letter of May 1989, and particularly after written expression of its policy in June 1989, would be unlawful fettering of discretion. (See e.g., Griffin v. Canada (Agriculture Can., Inspections Division) (1989), 39 Admin. L.R. 215 (F.C.T.D.); Lloyd v. Superintendent of Motor Vehicles, [1971] 3 W.W.R. 619, 20 D.L.R. (3d) 181 (B.C. C.A.); Re Lewis and Superintendent of Motor Vehicles for British Colombia (1980), 108 D.L.R. (3d) 525 (B.C. S.C.)). Similarly, it would be unlawful to refuse consideration of the Apotex bioavailability study for the reason, suggested at the hearing by counsel for the respondent, that it did not demonstrate equivalence of C (Can.) and C (U.S.), for the study was not submitted for that purpose and Apotex never suggested that it was. Finally, it would be unlawful to refuse for the reason, also alluded to at the hearing, that Apotex was simply seeking a convenient method of preparing a new drug submission, relying upon a study of Barr Laboratories, its affiliate in the U.S., rather than undertaking a study of its own. Surely convenient and efficient methods for seeking approval for a submission which meets the requirements of HPB should be encouraged, rather than discouraged, it seems to me. All of these reasons are irrelevant to the purposes for which the bioavailability study was submitted or to the purposes of the legislation.*
>
> . . .
>
> *This leads me to conclude that Apotex is entitled to have the bioavailability study reviewed in relation to assessment of the safety and effectiveness of Apo-A for marketing in Canada. It is relevant to that assessment and no lawful*

reason for refusing its review has been suggested. (See Oakwood, supra.)

- HPB's manner of dealing with Apotex was maladroit, at times dissembling. HPB was intransigent, and less than full and forthright. Having reviewed more evidence than Justice MacKay did, and having seen the witnesses in person, I find, unlike Justice MacKay, that HPB misled Apotex into a belief that HPB would be willing to receive further data and review it on a basis of equivalency. It was not. He wrote at para 90:

> *In the manner of its dealing with Apotex, HPB seems, in my view, to have been maladroit, at times dissembling if not actually misleading. I do not believe that it acted in bad faith or with malice. Nevertheless, it relied for a time on a "long-standing" policy, of which it could produce no written evidence antedating June 1989, after the Apo-A submission was initiated. HPB reached a settlement of the first application for judicial review undertaking "to consider evidence to establish equivalency between Canadian and non-Canadian reference standards" and later professed that there was no known methodology to establish this (presumably, aside from bioavailability studies directly comparing those two brands). It was intransigent in acknowledging it was satisfied of chemical equivalency of Canadian and U.S. reference standards until these proceedings were initiated and the matter heard; it failed to identify any particular dissatisfaction with dissolution studies, unlike its practice in other respects, until pleadings and discovery in these proceedings when its reservations were articulated. In my view it failed to reasonably explain other examples of accepted new drug submissions which relied upon bioavailability studies with reference to a foreign product, some approved after its enunciation and espousal of a policy that would preclude this. All these are instances of less than full and forthright dealing with Apotex. Perhaps these arose from some confusion or from re-organizations within HPB; perhaps some such circumstances are inevitable in a bureaucracy with its attendant difficulties of coordinating management of information and of people. But that does not excuse what must have seemed to Apotex a stubborn position supported over time by differing*

> *explanations. In short, had HPB's relationship with Apotex been more open and cooperative, while still setting HPB's own requirements with rational explanations, it is quite possible that the first application, or this one, for judicial review would not have been seen as necessary.*

After Justice MacKay's Decision

[72] In the beginning of 1993, Dann Michols moved from his position as an Assistant Deputy Minister at Health Canada to take over the responsibilities of the Drug Directorate for a period of time, as part of a reorganization going on in Health Canada. It was recognized that the processes within Health Canada were unconscionably slow, and were not as efficient as similar organizations in the United States, Britain and Europe.

[73] Under Michols' policies, including the use of a reference product, came under review, including consultation with "stakeholders". In December, 1995, a final policy was published requiring the comparator product to be a Canadian product already approved for sale in the Canadian market or another product meeting strict criteria. By that time, Apotex had received its NOC.

[74] I have no doubt that Michols' mandate was to shake up the bureaucracy at the Drug Directorate and get things done better. On October 7, 1993, Michols met with Dr. Sherman to discuss the Apo-Trazadone situation, following which, on October 12, he sent a very strong memorandum to Ms. Carman and Dr. Iain McGilveray stating in no uncertain terms that Apotex was owed a full explanation. That memorandum is worth repeating, as it is set out Michols

instructions in clear and unmistakable terms, with a copy sent to Health Canada's in-house lawyer, Mr. Stuart Archibald (Exhibit 8):

> *Apo-Trazadone*
>
> *As you know, I met with Barry Sherman on October 7, 1993 with our respective legal advisors on the subject of Apotex's submission for Apo-Trazadone.*
>
> *As a result, I have undertaken to write to Dr. Sherman, within the immediate future, a letter setting out:*
>
> 1. *The results of our review analysis of the dissolution data submitted by Apotex in as detailed a manner as possible, setting out any problems, deficiencies, etc. we may have with it.*
>
> 2. *Our decision on where the Apo-Trazadone submission stands, ie. Why we cannot issue an NOC, or if we believe we can, what more is required before we do.*
>
> *I appreciate that there are perhaps scientific subtleties in this file which I do not fully grasp but from a public policy perspective, we owe Apotex a full explanation of what the deficiencies in its submissions are. If these deficiencies are scientific, ie. dissolution data does not prove bioequivalency, then we should be prepared to say exactly why, or, if possible, how the deficiency analysis could be improved.*
>
> *If these deficiencies are of policy then we ought to be able to state definitively why we have the policy. Dr. Sherman gave several examples of cases where we have accepted dissolution data as the basis for a decision (Amoxi, Theophyline). If we can counter with a solid reaction as to why the cases were different, we should do so. If it comes down to our agreeing that Apotex did the correct studies and we agree with the results but simply believe that bioequivalency is not proved then we should quote a few cases that lead us to be uncertain (eg. Gemfibrozil, maybe?).*
>
> *I would appreciate it if you and Iain would work together to provide me with a draft letter to Dr. Sherman. I have the feeling that our practices and maybe even our policies have been inconsistent in the past. We have new management across the board. I would like clear signals on what our policies and practices will be.*

> *If I have not made myself clear on this matter, please call and we can discuss. I attach some documents that may be in the file but were given out at the meeting anyway. Once we have a draft that I understand, we will discuss with Stuart. You may want to involve Peter Jeffs in your discussions.*
>
> *Thank you for your dedication.*

[75] On January 14, 1994, Ms. Carman forwarded to Michols two different drafts of a letter that could be sent to Apotex. The thrust of the drafts was that dissolution data that had been submitted by Apotex could not be accepted as a means of establishing bioequivalence. Such a letter was never sent.

[76] HPB conducted a "re-review" of data previously submitted by Apotex. In a report from Mr. Ward, the evaluator, to Ms. Carman, dated April 8, 1994 (Exhibit 1, Tab 159), it was concluded that "*Apotex has not adequately established the bioequivalence of Canadian and U.S. Desyrel drug products*." That same day, Ms. Carman wrote to Apotex (Exhibit 1, Tab 159) stating that a Notice of Compliance would not be issued as a result of this re-review, and inviting Apotex to contact her to arrange a discussion between Apotex's technical people and the reviewer.

[77] The meeting took place on May 16, 1994 between Apotex's technical people and representatives of HPB. Minutes were kept (Exhibit 1, Tab 160). At that meeting Apotex undertook to conduct further dissolution studies and provide the results to HPB.

[78] The further studies were conducted and the results provided to HPB, Ms. Carman, by letter dated May 31, 1994 (Exhibit 1, Tab 162). The HPB reviewer, Mr. Ward, was immediately

put to the task of reviewing this material, and on June 23, 1994, he prepared what is referred to as a "draft" or "unsigned" report (Exhibit 1, Tab 164), in which Mr. Ward stated, *inter alia*:

> *DISCUSSION*
>
> *In light of the acknowledgement of chemical equivalence, the nature of the drug substance, and the results of comparative dissolution analyses in a variety of media over the physiological pH range, I have no outstanding concerns regarding the potential inequivalence of U.S. and Canadian marketed Desyrel.*
>
> . . .
>
> *CONCLUSION*
>
> *The purpose of this review was to evaluate the adequacy of data filed to establish the equivalence of U.S. and Canadian marketed Desyrel. In my opinion, Apotex has provided sufficient evidence to allay any reasonable concerns that said products could in general perform differently in vivo.*

[79] However, HPB did not communicate these findings to Apotex, even though it was quite aware that Apotex was anxious to hear the results. It appears that Mr. Ward sent a communication to Ms. Carman (Exhibit 1, Tab 167) saying that he was ready to meet with her before he went on holidays to discuss the draft. No such meeting took place. Ms. Carman does not know why; further, she could not recall receiving the draft.

[80] In mid-October, Apotex contacted Ms. Carman to see what was happening. She replied by voicemail that the matter was *"currently under discussion with legal counsel"* (Exhibit 1, Tab 172).

[81] An exchange of memoranda between Ms. Carman and Mr. Jeffs occurred (Exhibit 1, Tabs 173 and 175), in which Jeffs stated that *"we need to be very cautious";* Ms. Carman

expressed urgency and the need to *"provide guidance"*. On December 6, 1994, Ms. Carman wrote to Apotex (Exhibit 1, Tab 171) to say that a review was scheduled to commence December 15, 1994. Dr. Sherman wrote to Ms. Carman on December 19, 1994 (Exhibit 1, Tab 182), again expressing urgency.

[82] On December 16, 1994, Mr. Ward signed a report (Exhibit 1, Tab 199), which contained only slight revisions from his report dated June 23, 1994, and sent it to Ms. Carman This signed report stated the same findings as the June report:

> *DISCUSSION*
>
> *In light off the Crown's acknowledgement of chemical equivalence, the nature of the drug substance, and the results of comparative dissolution analyses in a variety of media over the physiological pH range, I conclude that no basis remains for articulating concerns regarding the potential inequivalence of U.S. and Canadian marketed Desyrel.*

[83] For unexplained reasons, Mr. Ward's report of December 16 was not sent to Ms. Carman until a week later – December 23 – in the result that, given the Christmas vacation, the report would not have been received until the New Year. When asked whether the delay in providing what was essentially the June 1994 report until the beginning of 1995 was fair to Apotex, Mr. Ward answered in one word: *"No."* (Transcript, page 785).

[84] On January 3, 1995, Ms. Carman had read the Ward report and sent a short note to him asking how they might extricate themselves from the matter. It is clear that she was worried as to potential consequences. She wrote (Exhibit 1, Tab 201):

> *I have read your report and do not see further difficulties presented…just the same old problems with how to extracate (sic) ourselves from this one. If you want to discuss, please drop by.*

[85] On January 6, 1995, Counsel from the Department of Justice, a Mr. Nagy, who had been junior counsel for the Crown in the judicial review heard by Justice MacKay, sent a peculiar letter to the lawyers for Apotex (Exhibit 1, Tab 103). It requested that Apotex sign a release, a draft of which was enclosed, releasing Her Majesty and others from *"any and all manner of claims, actions, causes of action, debts",* etc. The letter read:

> *Further to Ms. Mary Carman's letter to Apotex Inc. of December 6, 1994, Dr. Sherman*'s *responding letter to Ms. Carman of December 19, 1994, and my voice messages to you over the past three days, my client is attempting to expedite the review. It may be possible to finish the Apo-Trazadone review in less than the 120 days indicated in Ms. Carman's letter.*

[86] The implication of this letter is clear; Apotex is told that it may well get its NOC once the release is signed. I view this as an ill-advised, even bone-headed, attempt to "extricate" HPB from the problems created by this file.

[87] Senior Counsel at the Department of Justice quickly sought to distance HPB from this request following a letter of complaint from Apotex's lawyer of January 9, 1995 (Exhibit 1, Tab 204). On January 30, 1995, Ms. Thomas of the Department of Justice wrote (Exhibit 1, Tab 210), assuring Apotex's lawyers that she *"would not attempt to seek any agreements which would limit recourse which your client may properly have against mine".*

[88] Further deliberations took place between HPB and Apotex, causing Ms. Carman to write a handwritten note on a memorandum of 8 February 1995 (Exhibit 1, Tab 218), in effect saying to get on with it. She wrote:

> *We <u>are</u> or <u>are not</u> satisfied. I do not support continued clarifax requests.*

[89] Apotex got its NOC on February 28, 1995 (Exhibit 1, Tab 224).

<u>What does this Court make of the activity of Apotex and HPB post the Decision of Justice MacKay?</u>

[90] Following the release of the reasons of Justice MacKay January 19, 1993, Apotex continued to submit data to HPB directed to showing equivalence between the United States reference product and the Apotex product. This data was largely directed to dissolution rates, but it also included other matters, such as tablet hardness. Dr. Kibbe's unchallenged evidence (Exhibit 12, para 61), is that this material continued to support the equivalency of the Canadian and U.S. reference products. Apotex at no time backed down from using the U.S. reference product. At no time did Apotex submit results of any testing that it may have done using a Canadian reference product.

[91] Apotex continued to press HPB for a favourable decision. Apotex promptly answered all HPB requests. There is no delay attributable to Apotex in this respect.

[92] In the meantime, HPB was undergoing a significant re-organization. Efforts were led by Dr. Michols, and Ms. Carman, to vastly improve how that organization was run, and decisions

were made. They had much on their plate. Still, HPB had dragged its feet, involved legal counsel, tried to extricate itself and, sought a release from Apotex, all in a clumsy exercise to maintain a "policy" that it had agreed not to apply.

[93] It seems, however, that the wheels of a bureaucracy grind slowly. There continued to be procrastination, delay, unnecessary consultation, and the like. Some correspondence was copied to the in-house legal department or Department of Justice. Ms. Carman's telephone message of October 1994 makes it clear that lawyers were closely involved in this matter.

[94] The delay in dealing with Mr. Ward's findings of June 1994 until January 1995, which would largely have resolved the matter in Apotex's favour, remains unexplained.

[95] I find that there was a deliberate attempt to frustrate Apotex's submission for an NOC. There appears to have been endless circling around the internal idea that a Canadian reference product must be used, and the insistence that Apotex must prove the impossible – identicality.

[96] Ms. Carman's exasperated memo of 8 February 1992 "We <u>are</u> or <u>are not</u> satisfied" can be explained through the lens of Dr. Nitchuk's answer given in cross-examination at page 1149 of the transcript to the question *"Why do that?":*

> *Because we're a bureaucracy. I'm sorry. That's the reality.*

[97] The examination of the inner workings of HPB in this period is not pretty. Just as the saying attributed to Chancellor Bismarck, "Laws are like sausages, it is better not to see them

being made", it may have been better for HPB not to have its bureaucratic workings exposed. They were ugly.

After Apotex Got Its NOC

[98] There is little evidence as to what Apotex did after it got its NOC on February 28, 1995. In a letter dated March 23, 1995 (Exhibit 1, Tab 226), Apotex told HPB that it was currently marketing bottles of tablets in 50mg, 100mg and 150mg strength.

[99] On December 5, 1995, HPB published a Drug Directorate Policy regarding the use of a non-Canadian Reference Product (Exhibit 1, Tab 227). It set out a number of criteria to be met.

[100] On October 9, 1998, Apotex commenced the present action by filing a Statement of Claim with this Court. There is no evidence as to why it waited some three years after receiving its NOC, to do so.

[101] It has taken some sixteen years for this action to come to trial.

My Overall View of the Matter

[102] My overall view of the circumstances of this case is that Apotex was and still is a frequent "customer" of HPB. It, and in particular Dr. Sherman, are highly sophisticated in matters relating to HPB and the securing of NOC's to permit generic copies of drugs to be sold

in Canada. The nuances of these matters were well known to Apotex, and Apotex was not reluctant to push the envelope when it wanted to make a point.

[103] HPB was, particularly in the period up to 1993, an inefficient, badly run bureaucracy. It had unwritten policies, such as those respecting the use of non-Canadian reference drug products and whether or not third party files could be accessed in order to secure or confirm certain information. Even those internal policies were more in the nature of desiderata than firmly established policies; breaches, knowing and unknowing, occurred from time to time. HPB exhibited some of the worst features of bureaucracy; matters were recycled, nobody wanted to make a decision, endless consultation took place In particular, I am cautious concerning the evidence of Mr. Rowsell. His evidence given in the second judicial review - the one before Justice MacKay - shows that he does not pay sufficient attention to the accuracy of his sworn statements. Before me, he was rather quick to say that he reprimanded Dr. Nitchuk for a letter he wrote, something Dr Nitchuk vigorously denies. I expect Dr Nitchuk would remember a reprimand. I believe him and not Mr Rowsell.

[104] Mr Michols remembered in some detail in his evidence that he received a telephone call at home at about 11:00 p.m. from Dr. Sherman, who wanted to discuss matters respecting his submission. I expect that such a call, as well as persistent correspondence from Apotex, may well have irritated Michols. Apotex can be abrasive and aggressive. However, I do not attribute to Michols any deliberate attempt to frustrate Apotex in the course of its dealings with HPB.

[105] My clear sense of the matter, reviewing the evidence as a whole, is that Apotex wanted to make its Apo-Trazad submission a test case as to whether a non-Canadian drug product could be used a as a reference. Apotex readily performed tests using a Canadian reference respecting its Apo-Zidovudine product when it became clear that HPB was resisting the use of a non-Canadian reference. Dr. Sherman's evidence was that a Canadian reference could be used to test the Apo-Trazad product at a cost of a few hundred thousand dollars, and some months delay. Apotex, in fact, with respect to the Apo-Zidovudine, threatened to do just that with HPB, and then sue to recover the cost of testing and any loss of sales.

[106] Apotex's Counsel, in argument before me, cast aspersions on all of HPB's fact witnesses, including Mr. Rowsell. Counsel used words such as wongdoings, dishonest, invented a story, shamefully, false evidence, in addressing this evidence. I am not buying it. I would use words like careless and unconcerned about accuracy, about Mr. Rowsell; but as to the others, I accept that they tried their best to be honest, but somewhat embarrassed, about the facts and evidence as to what went on some twenty to twenty-eight years ago.

[107] Apotex knew what it was doing. It chose this as a test case. In no way was Apotex the victim that it purports to be.

[108] HPB was inefficient, hopelessly bureaucratic, dissembling and clumsy; as were, on occasion, its legal advisors.

Issues

[109] The basic issue is whether Apotex is entitled to recover damages, including punitive damages, for the failure to issue a Notice of Compliance to Apotex in respect of its Apo-Trazad drug until the lapse of an allegedly undue period of time of some seven years, and until after two generic competitors had been permitted to market their versions of the drug. I will accept that Apotex has shown that it may well have suffered damage in the nature of lost sales and loss of the ability to be the first or second generic in the marketplace. The quantum of such damages was not at issue before me; having been bifurcated by an Order of this Court, dated July 31, 2003. The issues before me relate to entitlement, if any, to damages.

[110] Apotex argues that it is entitled to damages based on one or more of the following causes of action:

- Misfeasance in public office;
- Negligence;
- Breach of contract (Settlement Agreement); and
- Misrepresentation (fraudulent, negligent, innocent).

[111] Her Majesty defends Apotex's claims on several grounds:

- Limitation Period bars the claim;
- There was no breach of the Settlement Agreement;

- Alternatively, the alleged breach of the Settlement Agreement was a result of ambiguous language in the contract;
- If there was a breach of the Settlement Agreement, Apotex had a duty to mitigate its damages;
- The negligence claim is statute barred;
- There was no duty of care owed to Apotex;
- There was no breach of the standard of care;
- There was no misrepresentation; whether fraudulent, negligent or innocent;
- There was no misfeasance in public office.

I. **Misfeasance in Public Office**

[112] Apotex makes several claims in tort; one of them is misfeasance in public office. This cause of action was thoroughly reviewed by the Supreme Court of Canada in *Odhavji Estate v Woodhouse* [2003] 3 SCR 263. I repeat a portion of the Reasons of that Court, written by Iacobucci J at paragraphs 18 to 32:

> *18 The origins of the tort of misfeasance in a public office can be traced to Ashby v. White (1703), 2 Ld. Raym. 938, 92 E.R. 126, in which Holt C.J. found that a cause of action lay against an elections officer who maliciously and fraudulently deprived Mr. White of the right to vote. Although the defendant possessed the power to deprive certain persons from participating in the election, he did not have the power to do so for an improper purpose. Although the original judgment suggests that he was [page279] simply applying the principle ubi jus ibi remedium, Holt C.J. produced a revised form of the judgment in which he stated that it was because fraud and malice were proven that the action lay: J. W. Smith, A Selection of Leading Cases on Various Branches of*

the Law (13th ed. 1929), at p. 282. Thus, in its earliest form it is arguable that misfeasance in a public office was limited to circumstances in which a public officer abused a power actually possessed.

19 Subsequent cases, however, have made clear that the ambit of the tort is not restricted in this manner. In Roncarelli v. Duplessis, [1959] S.C.R. 121, this Court found the defendant Premier of Quebec liable for directing the manager of the Quebec Liquor Commission to revoke the plaintiff's liquor licence. Although Roncarelli was decided at least in part on the basis of the Quebec civil law of delictual responsibility, it is widely regarded as having established that misfeasance in a public office is a recognized tort in Canada. See for example Powder Mountain Resorts Ltd. v. British Columbia (2001), 94 B.C.L.R. (3d) 14, 2001 BCCA 619; and Alberta (Minister of Public Works, Supply and Services) v. Nilsson (2002), 220 D.L.R. (4th) 474, 2002 ABCA 283. In Roncarelli, the Premier was authorized to give advice to the Commission in respect of any legal questions that might arise, but had no authority to involve himself in a decision to revoke a particular licence. As Abbott J. observed, at p. 184, Mr. Duplessis "was given no statutory power to interfere in the administration or direction of the Quebec Liquor Commission". Martland J. made a similar observation, at p. 158, stating that Mr. Duplessis' conduct involved "the exercise of powers which, in law, he did not possess at all". From this, it is clear that the tort is not restricted to the abuse of a statutory or prerogative power actually held. If that were the case, there would have been no grounds on which to find Mr. Duplessis liable.

[page280]

20 This understanding of the tort is consistent with the widespread consensus in other common law jurisdictions that there is a broad range of misconduct that can found an action for misfeasance in a public office. For example, in Northern Territory of Australia v. Mengel (1995), 129 A.L.R. 1 (H.C.), Brennan J. wrote as follows, at p. 25:

> *The tort is not limited to an abuse of office by exercise of a statutory power. Henly v. Mayor of Lyme [(1828), 5 Bing. 91, 130 E.R. 995] was not a case arising from an impugned exercise of a statutory power. It arose from an alleged failure to maintain a sea wall or bank, the maintenance of which was a condition of the grant to the corporation of Lyme of the sea wall or bank and the*

> *appurtenant right to tolls. Any act or omission done or made by a public official in the purported performance of the functions of the office can found an action for misfeasance in public office. [Emphasis added.]*

In Garrett v. Attorney-General, [1997] 2 N.Z.L.R. 332, the Court of Appeal for New Zealand considered an allegation that a sergeant failed to investigate properly the plaintiff's claim that she had been sexually assaulted by a police constable. Blanchard J. concluded, at p. 344, that the tort can be committed "by an official who acts or omits to act in breach of duty knowing about the breach and also knowing harm or loss is thereby likely to be occasioned to the plaintiff".

21 The House of Lords reached the same conclusion in Three Rivers District Council v. Bank of England (No. 3), [2000] 2 W.L.R. 1220. In Three Rivers, the plaintiffs alleged that officers with the Bank of England improperly issued a licence to the Bank of Credit and Commerce International and then failed to close the bank once it became evident that such action was necessary. Forced to consider whether the tort could apply in the case of omissions, the House of Lords concluded that "the tort can be constituted by an omission by a public officer as well as by acts on his part" (per Lord Hutton, at p. 1267). In Australia, New Zealand and the United Kingdom, it is equally clear that the tort of misfeasance is not limited to the unlawful [page281] exercise of a statutory or prerogative power actually held.

22 What then are the essential ingredients of the tort, at least insofar as it is necessary to determine the issues that arise on the pleadings in this case? In Three Rivers, the House of Lords held that the tort of misfeasance in a public office can arise in one of two ways, what I shall call Category A and Category B. Category A involves conduct that is specifically intended to injure a person or class of persons. Category B involves a public officer who acts with knowledge both that she or he has no power to do the act complained of and that the act is likely to injure the plaintiff. This understanding of the tort has been endorsed by a number of Canadian courts: see for example Powder Mountain Resorts, supra; Alberta (Minister of Public Works, Supply and Services) (C.A.), supra; and Granite Power Corp. v. Ontario, [2002] O.J. No. 2188 (QL) (S.C.J.). It is important, however, to recall that the two categories merely represent two different ways in which a public officer can commit the tort; in each instance, the plaintiff must prove each of the tort's constituent elements. It is thus

necessary to consider the elements that are common to each form of the tort.

23 In my view, there are two such elements. First, the public officer must have engaged in deliberate and unlawful conduct in his or her capacity as a public officer. Second, the public officer must have been aware both that his or her conduct was unlawful and that it was likely to harm the plaintiff. What distinguishes one form of misfeasance in a public office from the other is the manner in which the plaintiff proves each ingredient of the tort. In Category B, the plaintiff must prove the two ingredients of the tort independently of one another. In Category A, the fact that the public officer has acted for the express purpose of harming the plaintiff is sufficient to satisfy each ingredient of the tort, owing to the fact that a public officer does not have the authority to exercise his or her powers for an improper purpose, such [page282] as deliberately harming a member of the public. In each instance, the tort involves deliberate disregard of official duty coupled with knowledge that the misconduct is likely to injure the plaintiff.

24 Insofar as the nature of the misconduct is concerned, the essential question to be determined is not whether the officer has unlawfully exercised a power actually possessed, but whether the alleged misconduct is deliberate and unlawful. As Lord Hobhouse wrote in Three Rivers, supra, at p. 1269:

> *The relevant act (or omission, in the sense described) must be unlawful. This may arise from a straightforward breach of the relevant statutory provisions or from acting in excess of the powers granted or for an improper purpose.*

Lord Millett reached a similar conclusion, namely, that a failure to act can amount to misfeasance in a public office, but only in those circumstances in which the public officer is under a legal obligation to act. Lord Hobhouse stated the principle in the following terms, at p. 1269: "If there is a legal duty to act and the decision not to act amounts to an unlawful breach of that legal duty, the omission can amount to misfeasance [in a public office]." See also R. v. Dytham, [1979] Q.B. 722 (C.A.). So, in the United Kingdom, a failure to act can constitute misfeasance in a public office, but only if the failure to act constitutes a deliberate breach of official duty.

25 Canadian courts also have made a deliberate unlawful act a focal point of the inquiry. In Alberta (Minister of Public Works, Supply and Services) v. Nilsson (1999), 70 Alta. L.R. (3d) 267,

1999 ABQB 440, at para. 108, the Court of Queen's Bench stated that the essential question to be determined is whether there has been deliberate misconduct on the part of a public official. Deliberate misconduct, on this view, consists of: (i) an intentional illegal act; and (ii) an intent to harm an individual or class [page283] of individuals. See also Uni-Jet Industrial Pipe Ltd. v. Canada (Attorney General) (2001), 156 Man. R. (2d) 14, 2001 MBCA 40, in which Kroft J.A. adopted the same test. In Powder Mountain Resorts, supra, Newbury J.A. described the tort in similar terms, at para. 7:

> *... it may, I think, now be accepted that the tort of abuse of public office will be made out in Canada where a public official is shown either to have exercised power for the specific purpose of injuring the plaintiff (i.e., to have acted in "bad faith in the sense of the exercise of public power for an improper or ulterior motive") or to have acted "unlawfully with a mind of reckless indifference to the illegality of his act" and to the probability of injury to the plaintiff. (See Lord Steyn in Three Rivers, at [1231].) Thus there remains what in theory at least is a clear line between this tort on the one hand, and what on the other hand may be called negligent excess of power -- i.e., an act committed without knowledge of (or subjective recklessness as to) its unlawfulness and the probable consequences for the plaintiff. [Emphasis in original.]*

Under this view, the ambit of the tort is limited not by the requirement that the defendant must have been engaged in a particular type of unlawful conduct, but by the requirement that the unlawful conduct must have been deliberate and the defendant must have been aware that the unlawful conduct was likely to harm the plaintiff.

26 As is often the case, there are a number of phrases that might be used to describe the essence of the tort. In Garrett, supra, Blanchard J. stated, at p. 350, that "[t]he purpose behind the imposition of this form of tortious liability is to prevent the deliberate injuring of members of the public by deliberate disregard of official duty." In Three Rivers, supra, Lord Steyn stated, at p. 1230, that "[t]he rationale of the tort is that in a legal system based on the rule of law executive or administrative power 'may be exercised only for the public good' and not for ulterior and improper purposes." As each passage makes clear, misfeasance in

a public office is not directed at a public officer who inadvertently or negligently fails adequately to discharge the obligations of his or her office: see Three Rivers, at p. 1273, per Lord [page284] Millett. Nor is the tort directed at a public officer who fails adequately to discharge the obligations of the office as a consequence of budgetary constraints or other factors beyond his or her control. A public officer who cannot adequately discharge his or her duties because of budgetary constraints has not deliberately disregarded his or her official duties. The tort is not directed at a public officer who is unable to discharge his or her obligations because of factors beyond his or her control but, rather, at a public officer who could have discharged his or her public obligations, yet wilfully chose to do otherwise.

27 Another factor that may remove an official's conduct from the scope of the tort of misfeasance in a public office is a conflict with the officer's statutory obligations and his or her constitutionally protected rights, such as the right against self-incrimination. Should such circumstances arise, a public officer's decision not to comply with his or her statutory obligation may not amount to misfeasance in a public office. I need not decide that question here except that it could be argued. A public officer who properly insists on asserting his or her constitutional rights cannot accurately be said to have deliberately disregarded the legal obligations of his or her office. Under this argument, an obligation inconsistent with the officer's constitutional rights is not itself lawful.

28 As a matter of policy, I do not believe that it is necessary to place any further restrictions on the ambit of the tort. The requirement that the defendant must have been aware that his or her conduct was unlawful reflects the well-established principle that misfeasance in a public office requires an element of "bad faith" or "dishonesty". In a democracy, public officers must retain the authority to make decisions that, where appropriate, are adverse to the interests of certain citizens. Knowledge of harm is thus an insufficient basis on which to conclude that the defendant has acted in bad faith or dishonestly. A [page285] public officer may in good faith make a decision that she or he knows to be adverse to interests of certain members of the public. In order for the conduct to fall within the scope of the tort, the officer must deliberately engage in conduct that he or she knows to be inconsistent with the obligations of the office.

29 The requirement that the defendant must have been aware that his or her unlawful conduct would harm the plaintiff further restricts the ambit of the tort. Liability does not attach to each officer who blatantly disregards his or her official duty, but only to

a public officer who, in addition, demonstrates a conscious disregard for the interests of those who will be affected by the misconduct in question. This requirement establishes the required nexus between the parties. Unlawful conduct in the exercise of public functions is a public wrong, but absent some awareness of harm there is no basis on which to conclude that the defendant has breached an obligation that she or he owes to the plaintiff, as an individual. And absent the breach of an obligation that the defendant owes to the plaintiff, there can be no liability in tort.

30 In sum, I believe that the underlying purpose of the tort is to protect each citizen's reasonable expectation that a public officer will not intentionally injure a member of the public through deliberate and unlawful conduct in the exercise of public functions. Once these requirements have been satisfied, it is unclear why the tort would be restricted to a public officer who engaged in the unlawful exercise of a statutory power that she or he actually possesses. If the tort were restricted in this manner, the tort would not extend to a public officer, such as Mr. Duplessis, who intentionally exceeded his powers for the express purpose of interfering with a citizen's economic interests. Nor would it extend to a public officer who breached a statutory obligation for the same purpose. But there is no principled reason, in my view, why a public officer who wilfully injures a member of the public [page286] through intentional abuse of a statutory power would be liable, but not a public officer who wilfully injures a member of the public through an intentional excess of power or a deliberate failure to discharge a statutory duty. In each instance, the alleged misconduct is equally inconsistent with the obligation of a public officer not to intentionally injure a member of the public through deliberate and unlawful conduct in the exercise of public functions.

31 I wish to stress that this conclusion is not inconsistent with R. v. Saskatchewan Wheat Pool, [1983] 1 S.C.R. 205, in which the Court established that the nominate tort of statutory breach does not exist. Saskatchewan Wheat Pool states only that it is insufficient that the defendant has breached the statute. It does not, however, establish that the breach of a statute cannot give rise to liability if the constituent elements of tortious responsibility have been satisfied. Put a different way, the mere fact that the alleged misconduct also constitutes a breach of statute is insufficient to exempt the officer from civil liability. Just as a public officer who breaches a statute might be liable for negligence, so too might a public officer who breaches a statute be liable for misfeasance in a public office. Saskatchewan Wheat Pool would only be relevant to this motion if the appellants had pleaded no more than a failure to discharge a statutory obligation. This, however, is not the case.

> *The principle established in Saskatchewan Wheat Pool has no bearing on the outcome of the motion on this appeal.*
>
> *32 To summarize, I am of the opinion that the tort of misfeasance in a public office is an intentional tort whose distinguishing elements are twofold: (i) deliberate unlawful conduct in the exercise of public functions; and (ii) awareness that the conduct is unlawful and likely to injure the plaintiff. Alongside deliberate unlawful conduct and the requisite knowledge, a plaintiff must also prove the other requirements common to all torts. More specifically, [page287] the plaintiff must prove that the tortious conduct was the legal cause of his or her injuries, and that the injuries suffered are compensable in tort law.*

[113] Thus, the tort of misfeasance of public office must, in addition to the usual elements of tort, include:

i deliberate unlawful conduct in the exercise of public functions; and

ii awareness that the conduct is unlawful and likely to injure the Plaintiff.

[114] The Ontario Court of Appeal has stated that misfeasance in public office need not be committed by a single individual; it can be committed by a group of individuals. Rouleau JA, for the Court, in *O'Dwyer v Ontario Racing Commission*, 2008 ONCA 446, 293 DLR (4th) 559, wrote at paragraph 43:

> *43 The requirement that the tort be committed by a "public officer" was addressed in the seminal case of Three Rivers D.C. v. Bank of England (No. 3), [2000] 2 W.L.R. 1220, in which the House of Lords commented that public office is to be defined in "a relatively wide sense". The decision in Jones v. Swansea City Council, [1990] 1 W.L.R. 1453 (C.A.), was cited for the purpose of demonstrating that a collective public body such as a council can be liable for the tort. The decision in Three Rivers was largely adopted into Canadian law through the Supreme Court decision in Odhavji Estate v. Woodhouse.*

[115] The nature of the "unlawful" act set out in the *Odhavji* test encompasses a "broad range" of misconduct as stated by Iacobucci J at paragraph 20 above.

[116] In this Court, Prothonotary Aalto has considered the tort of misfeasance in *McMaster v Canada*, 2008 FC 1158, 336 FTR 92; his decision was affirmed by Mandamin J, 2009 FC 937, 352 FTR 255, at paragraph 66. In that case, the Plaintiff was incarcerated in a federal prison and required special shoes. The prison officials procrastinated. Prothonotary Aalto held that those officials had committed a misfeasance in public office. He wrote at paragraphs 51 and 52:

> *51 Counsel for the Defendant argued that the Plaintiff had to prove that both Ms. Allen and Ms. Wherry must have had the intent to act unlawfully. In my view, there is no such requirement. The actions of Ms. Wherry are sufficient to ground the cause of action.*
>
> *52 Counsel for the Defendant argued vociferously that the Defendant made reasonable efforts to satisfy the Plaintiff's request for shoes as they were ordered three times and that the Defendant did not know the old shoes were worn out. I disagree. The evidence shows that the Defendant dragged its feet in ordering the correct shoes for the Plaintiff and improperly tried to convince the Plaintiff to accept the ill-fitting shoes when it obviously knew they did not and could not fit. Further, the Directive requires that the Plaintiff be issued new shoes on an annual basis. The Plaintiff requisitioned his new shoes because his old ones were over a year old. Ms. Wherry knew this to be the case.*

[117] In the circumstances of the present case, I find that HPB knew since the date of the Settlement Agreement that they were to consider Apotex's submissions on the basis of equivalency. They ignored that requirement; they stuck to an internal notion of identicality. Further, there was an effort by HPB to conceal this notion from Apotex.

[118] I find that:

i Upon entering into the Settlement Agreement with Apotex, HPB acted in bad faith by engaging in a deliberate exercise of conducting its examination of Apotex's submissions on the basis of identicality, notwithstanding its undertaking to do otherwise; and

ii HPB were quite aware that a delay or refusal to accept Apotex's submissions would be likely to injure Apotex, given Dr. Sherman's repeated warnings to HPB of the same.

[119] The case of misfeasance in public office by the Defendant's officials has been made out.

Negligence

[120] Apotex alleges that HPB was negligent. The Defendant argues, relying on Binnie J's judgment for the Supreme Court of Canada in *Canada (Attorney General) v TeleZone Inc*, [2010] 3 SCR 585 at paragraph 69, that governments make discretionary decisions all the time, which will reflect losses on people and businesses without giving rise to causes of action known to the law.

[121] However, there is a cause of action respecting negligence by government officials. It is called the *Cooper/Anns* test. The Supreme Court of Canada in *Cooper v Hobart*, [2001] 3 SCR 537 considered this test in detail. I summarized that test in *Gordon v Canada*, 2013 FC 597 at paragraphs 23 to 25:

23 Both parties agree that a cause of action in respect of negligence in these circumstances is to be examined on the basis of what is described as the Anns/Cooper test. That test originated in the House of Lords decision of Anns v Merton London Borough Council, [1978] AC 728 and was further developed by the Supreme Court of Canada in Cooper v Hobart, [2001] 3 SCR 537. The test may be succinctly stated as a two-stage test where, if the answer to the first question is yes, then the Court must move on to consider the second question; but, if the answer to the first question is no, then there is no need to consider the second question. The questions are:

> *1. Is there a sufficient proximity between the party alleged to have been negligent and the party alleged to have been injured so as to create a duty of care? If the answer is yes, then:*
>
> *2. Are there policy considerations which would negate the creation of a duty of care in the circumstances of the case?*

24 As to the first question, McLachlin CJ and Major J for the Supreme Court in Cooper wrote at paragraph 35:

> *35 The factors which may satisfy the requirement of proximity are diverse and depend on the circumstances of the case. One searches in vain for a single unifying characteristic. As stated by McLachlin J. (as she then was) in Canadian National Railway Co. v. Norsk Pacific Steamship Co., [1992] 1 S.C.R. 1021, at p. 1151: "[p]roximity may be usefully viewed, not so much as a test in itself, but as a broad concept which is capable of subsuming different categories of cases involving different factors" (cited with approval in Hercules Managements, [1997] 2 S.C.R. 165, supra, at para. 23). Lord Goff made the same point in Davis v. Radcliffe, [1990] 2 All E.R. 536 (P.C.), at p. 540:*
>
> > *... it is not desirable, at least in the present stage of development of the law, to attempt to state in broad general propositions the circumstances in which such proximity may or may not be held to exist. On the contrary, following the expression of opinion by Brennan J in Sutherland Shire Council v Heyman (1985) 60 ALR 1 at 43-44, it is*

> *considered preferable that 'the law should develop categories of negligence incrementally and by analogy with established categories'.*

25 As to the second question, they wrote at paragraph 37:

> *37 This brings us to the second stage of the Anns test. As the majority of this Court held in Norsk, at p. 1155, residual policy considerations fall to be considered here. These are not concerned with the relationship between the parties, but with the effect of recognizing a duty of care on other legal obligations, the legal system and society more generally. Does the law already provide a remedy? Would recognition of the duty of care create the spectre of unlimited liability to an unlimited class? Are there other reasons of broad policy that suggest that the duty of care should not be recognized? Following this approach, this Court declined to find liability in Hercules Managements, supra, on the ground that to recognize a duty of care would raise the spectre of liability to an indeterminate class of people.*

[122] There are decisions by a number of Courts dealing with various fact situations in which the *Cooper/Anns* test may or may not apply. At one end there was imposed a duty upon an investigating police officer in *Hill v Hamilton-Wentworth Regional Police Services Board*, [2007] 3 SCR 129; at the other end a government food inspector did not owe a duty to sellers of food products respecting the alleged negligent inspection leading to the destruction of the sellers' carrots; *Los Angeles Salad Co v Canadian Food Inspection Agency*, 2013 BCCA 34, 358 DLR (4th) 581.

[123] Here, were it not for the Settlement Agreement, I would find that HPB was not in a position where it owed a duty of care to Apotex over and above any duty owed to any other

pharmaceutical company seeking approval to sell a drug in Canada. However, the Settlement Agreement changed all that. By stating to Apotex that it would examine Apotex's submissions on the basis of equivalency, HPB put itself in a special relationship with Apotex and owed a duty of care not only to examine Apotex's submissions on that standard, but also to be open and transparent as to what it had done (*Central Trust Co v Rafuse*, [1986] 2 SCR 147 at para 49). HPB failed on both counts and acted negligently in doing so, I address the standard of care below. The answer to the first of the *Cooper/Anns* questions is yes.

[124] The second of the *Cooper/Anns* questions is to ask whether there are any policy considerations whereby liability should not be imposed on HPB. The Defendant submitted two policy considerations to negate the duty (1) HPB applied its broad discretion under the *Food and Drugs Act* and *Regulations* in the area of public policy related to the health and safety of the public when deciding whether to issue the NOC, and Apotex cannot challenge the exercise of this discretion; (2) Finding a duty would expose the Crown to indeterminate liability.

[125] On first policy consideration, it is true that HPB was considering the "policy" of safety and efficacy when it examined Apotex's submission. It is also true that the Minister has a measure of discretion when formulating policy. But that is not the issue here.

[126] The issue here is whether there is any core policy whereby HPB should be relieved from a finding of negligence, in which it agreed to do one thing, but did another, and attempted to conceal or dissemble that fact. There is no such policy against this irrational conduct taken in bad faith (*R v Imperial Tobacco Canada Ltd*, [2011] 3 SCR 45 at para 90).

[127] On the second policy consideration, no such threat of indeterminate liability exists here. HPB chose to enter into the Settlement Agreement with Apotex to end the first judicial review and thus create a special relationship with Apotex. The liability that arises is unique to this case and would not open the door to indeterminate liability unless the government makes the choice to conduct itself in the manner that it did in this case. Instead a finding of liability in this case would support the policy objective of ensuring the Crown does not negligently breach an undertaking to a party to act in a certain way in order to induce that party to abandon a legal proceeding against the Crown.

[128] On whether HPB breached the standard of care, the Defendant argued that Apotex merely alleged that the Crown made an administrative law error which did not constitute a private law fault. HPB did not breach the standard of care because it acted within its broad discretion to require information and materials deemed necessary and had a solid scientific basis for requesting a Canadian reference product. This argument fails for the same reason that Crown's argument that no duty of care existed failed. The Crown through the Settlement Agreement bound itself to a standard of exercising its discretion based on an equivalency standard. Its continued request for a Canadian reference standard in the face of evidence that proved equivalence between Canadian and U.S. Desyrel products represented its adherence to a standard of identicality. This adherence to identicality constituted negligence.

[129] On causation, the Defendant argued Apotex was the cause of its loss by attempting to use Apo-Trazad as a test case to force HPB to use a foreign reference standard in the future submissions. Hence Apotex knowingly took the risk of suffering loss of incoming including not

being the first generic to market and the taxpayer should not be liable for this choice. I agree with this argument up until the parties entered the Settlement Agreement. Prior to the Settlement Agreement HPB required Apotex to use a Canadian Reference product as it did in the past, and Apotex chose to persuade HPB to pursue another avenue of eligibility. However, once HPB entered into the Settlement Agreement it established a duty of care towards Apotex and it was reasonable for Apotex to expect that the Crown would not breach this duty. This breach of duty caused Apotex's loss. Apotex's failure to conduct a Canadian reference study subsequent to entering the Settlement Agreement is relevant to the issue of mitigation of damages, not whether the Crown's adherence to an identicality standard caused Apotex's loss. I address mitigation issues later in my Reasons.

[130] While no party discussed remoteness in the hearing, I find that Apotex's damages were not remote, it was reasonably foreseeable that delaying issuing the NOC would cause Apotex damages in the form of lost sales and by preventing Apotex from being the first to the market.

[131] I therefore find that the Defendant is liable for negligence.

Misrepresentation

[132] Apotex alleges that HPB made misrepresentations either deliberately or negligently. Those misrepresentations are not freestanding, but part of the misfeasance and negligence that I have already addressed. There is no need to ground Apotex's claim to damages on yet another aspect of the law of tort.

Breach of Contract – the Settlement Agreement

[133] Apotex asserts that HPB broke the Settlement Agreement by continuing to insist, internally, upon a standard of identicality in dealing with bioequivalence, rather than equivalency as promised in the Settlement Agreement. Further, Apotex asserts, HPB misled Apotex by stating that it was applying an equivalency standard; whereas, in fact, it was not. I fully agree.

[134] Defendant's Counsel argues that the use of the word equivalency in the Settlement Agreement was ambiguous. As I have stated earlier in these Reasons, it was not. Counsel also argued that HPB in fact applied an equivalency standard. It did not, it applied the identicality test.

[135] However, as I will discuss shortly, Apotex's claim for breach of contract is barred by a limitation period as pleaded by the Defendant.

Limitation Period

[136] The Defendant has pleaded the provisions of the *Limitations Act*, RSO 1990, Chapter L.15; in particular, Section 45 which, by virtue of section 39 of the *Federal Courts Act*, RSC 1985, c. F-7, applies to the parties; both of whom are situated in Ontario. However, those provisions have only been pleaded in respect of the claim made by Apotex in contract. As Counsel for the Defendant admitted, no such pleading was made in respect of any of Apotex's various claims in tort. It is trite law, going as far back as Audette J's judgment in *R v L'Heureux*

(1913), 14 Ex CR 250 at 253-254, 14 DLR 604 that a party must plead a limitations defence in order to rely upon it (see also, *Kibale v Canada*, [1990] FCJ No 1079 at para 3 (CA).

[137] Here, the applicable limitations period is six years before this action was commenced. This action was commenced on October 9, 1998; therefore, any claim respecting breach of contract occurring before October 9, 1992 would be extinguished by the effect of the *Limitation Act*, supra, provided that Apotex knew or ought to have known of the breach.

[138] The contract at issue is the Settlement Agreement signed by HPB's lawyer and delivered to Apotex November 26, 1990. Almost immediately HPB broke the terms off the Agreement. It continued to deal with Apotex's submissions on an "identicality" standard, rather than on an "equivalency" standard; notwithstanding the Agreement to the contrary. Apotex could not have known this at the beginning; however, it is clear that by April 1991, as evidenced by the letters written by Apotex to HPB on April 25, 1991 and July 2 and 31, 1991, in April and July of that year as reviewed earlier in these Reasons, Apotex was aware and possessed sufficient facts to be aware that HPB was acting in breach of the Settlement Agreement and that Apotex was suffering damage as a result (Exhibit 1, Tabs 83, 102 and 111).

[139] Apotex's Counsel makes a nuanced argument to the effect that it was not until Justice MacKay delivered his decision on January 19, 1993, did Apotex became aware and appreciate the full nature and extent of HPB's dealings. I reject this argument. The law is clear that the time that a person ought to have known of a wrongdoing is when they became aware of some damage, even though the nature and extent of the wrongdoing was not fully apparent to them.

[140] The leading case on point is the decision of the Supreme Court of Canada in *Peixeiro v Haberman*, [1997] 3 SCR 549, where Major J, for the Court, wrote at paragraph 18:

> *18 It was conceded that at common law ignorance of or mistake as to the extent of damages does not delay time under a limitation period. The authorities are clear that the exact extent of the loss of the plaintiff need not be known for the cause of action to accrue. Once the plaintiff knows that some damage has occurred and has identified the tortfeasor (see Cartledge v. E. Jopling & Sons Ltd., [1963] A.C. 758 (H.L.), at p. 772 per Lord Reid, and July v. Neal (1986), 57 O.R. (2d) 129 (C.A.)), the cause of action has accrued. Neither the extent of damage nor the type of damage need be known. To hold otherwise would inject too much uncertainty into cases where the full scope of the damages may not be ascertained for an extended time beyond the general limitation period.*

[141] The Supreme Court repeated this principle in *Ryan v Moore*, [2005] 2 SCR 53, where Bastarache J, for the Court, wrote at paragraphs 21 to 23:

> *21 The debate concerning the use of the discoverability principle in tort actions has been settled by this Court in Kamloops (City of) v. Nielsen, [1984] 2 S.C.R. 2, Central Trust and M. (K.) v. M. (H.), [1992] 3 S.C.R. 6.*
>
> *22 The discoverability principle provides that "a cause of action arises for purposes of a limitation period when the material facts on which it is based have been discovered or ought to have been discovered by the plaintiff by the exercise of reasonable diligence": Central Trust, at p. 224. In some provinces, the discoverability rule has been codified by statute; in others, it has been deemed redundant because of other remedial provisions.*
>
> *23 While discoverability has been qualified in the past as a "general rule" (Central Trust, at p. 224; Peixeiro v. Haberman, [1997] 3 S.C.R. 549, at [page68] para. 36), it must not be applied systematically without a thorough balancing of competing interests (Peixeiro, at para. 34). The rule is an interpretative tool for construing limitation statutes. I agree with the Manitoba Court of Appeal when it writes:*
>
> > *In my opinion, the judge-made discoverability rule is nothing more than a rule of construction. Whenever a statute requires an action to be*

> *commenced within a specified time from the happening of a specific event, the statutory language must be construed. When time runs from "the accrual of the cause of action" or from some other event which can be construed as occurring only when the injured party has knowledge of the injury sustained, the judge-made discoverability rule applies. But, when time runs from an event which clearly occurs without regard to the injured party's knowledge, the judge-made discoverability rule may not extend the period the legislature has prescribed. [Emphasis added.]*
>
> (Fehr v. Jacob (1993), 14 C.C.L.T. (2d) 200, at p. 206)

See also Peixeiro, at para. 37; Snow v. Kashyap (1995), 125 Nfld. & P.E.I.R. 182 (Nfld. C.A.).

[142] Ducharme J's decision in *Calgar v Moore*, [2005] OJ No 4606 at para 24, 143 ACWS (3d) 754 (Sup Ct) discusses the applicability of the discoverability principle to contract law:

> *24 Under the discoverability principle, a cause of action arises for the purposes of a limitation period when the material facts upon which it is based have been discovered by the plaintiff or ought to have been discovered by the plaintiff by the exercise of reasonable diligence. This is an objective test and the plaintiff is not required to have discovered all the facts upon which his or her action is based. The discoverability rule applies to claims in contract and in tort. Thus, an action for breach of contract commences when the plaintiff has sufficient facts to recognize that the contract has been breached [emphasis added]. The plaintiff is not required to have sustained or be in a position to assess damages before being able to sue. Error or ignorance of the law does not postpone any limitation period.*

[143] I find, therefore, that Apotex's claim in contract, but not its claims in tort, are extinguished by the limitations period as pleaded.

Repudiation

[144] The Defendant argues that Apotex cannot make a claim based on the Settlement Agreement. It is argued that the consideration received by HPB for the Settlement Agreement was Apotex's forbearance in bringing or continuing legal proceedings for judicial review. Once Apotex commenced the second judicial review, there was a failure of consideration, the Agreement had been repudiated.

[145] Repudiation has not been pleaded by the Defendant. The first time it was raised was a brief mention in Defendant's Counsel's opening statement.

[146] As with the limitation defence for negligence, I find that repudiation, as a defence, should have been pleaded; it was not. Therefore, it is not available to the Defendant as a defence to the action in contract.

When Do Apotex's Damages Begin to Accrue

[147] Apotex is entitled to be put in the position that it would have been were it not for the wrongful acts of the Defendant. Apotex is entitled to receive the profits, if any, that it would have received from the sale of its Apo-Trazad product commencing at a date when it reasonably could have expected to receive its Notice of Compliance, to the date when it actually received that Notice. The profits that might have been made must be offset by the profits that Apotex might have received, had it mitigated its damages; a subject which I will address shortly.

[148] The evidence of Dr. Simon is that in the period 1988 to 1995 and beyond, there was considerable backlog at HPB (Transcript page 626). The evidence of Dr. Sherman is that, if Apotex had "capitulated" to HPB's request for a Canadian reference product, they would have submitted the data by the end of 1990 and they could have received their NOC before the other generics (Transcript pages 345 to 347). He said that he would have expected to get an NOC in about a year, when Apotex filed its submission in 1988, but that he did not know what the effect of a backlog might be; instead; Apotex brought its first judicial review application in August 1990 (Transcript pages 348 to 353). As soon as Apotex brought that judicial review application, Dr. Sherman testified that settlement discussions commenced; and, according to Dr. Sherman, HPB abandoned its position and agreed to review Apotex's submission based on a bio-study equivalent (Transcript pages 353 to 363).

[149] I have founded my decision respecting liability in tort based on HPB's representations in the Settlement Agreement and failure of HPB to follow through upon its commitments. I find that is reasonable, therefore, to use the date of the Settlement Agreement as the date upon which HPB should have examined Apotex's submission and add to that one year to arrive at the date upon which Apotex should have received its NOC. Therefore, I establish November 26, 1991 as the date upon which Apotex should have received its NOC.

Mitigation

[150] The Defendant argues that, even if it is liable in contract or tort, the Plaintiff failed to mitigate its losses. The Plaintiff argues that if the Crown means that it should have tested its product against a Canadian reference standard, then that would not have been mitigation, but

capitulation. In any event, the Plaintiff argues that it did seek to mitigate its losses by instituting and prosecuting the second judicial review as soon as it was reasonably aware that HPB would not change its mind concerning the use of a Canadian reference standard; or, in the alternative, would not accept that a non-Canadian reference product should be evaluated against a standard of equivalency.

[151] The basic principle of mitigation is that while a wronged Plaintiff must prove its damages, the Plaintiff is required to take reasonable steps to avoid the unreasonable accumulation of those damages. The fundamental decision in this regard is that of the Supreme Court of Canada in *Michaels v Red Deer College*, [1976] 2 SCR 324, in which Laskin CJ for the majority, wrote at paragraphs 9 to 12:

> *It is, of course, for a wronged plaintiff to prove his damages, and there is therefore a burden upon him to establish on a balance of probabilities what his loss is. The parameters of loss are governed by legal principle. The primary rule in breach of contract cases, that a wronged plaintiff is entitled to be put in as good a position as he would have been in if there had been proper performance by the defendant, is subject to the qualification that the defendant cannot be called upon to pay for avoidable losses which would result in an increase in the quantum of damages payable to the plaintiff. The reference in the case law to a "duty" to mitigate should be understood in this sense.*
>
> *In short, a wronged plaintiff is entitled to recover damages for the losses he has suffered but the extent of those losses may depend on whether he has taken reasonable steps to avoid their unreasonable accumulation. In Payzu Ltd. v. Saunders [[1919] 2 K.B. 581.], at p. 589, Scrutton L.J. explained the matter in this way:*
>
> > *Whether it be more correct to say that a plaintiff must minimize his damages, or to say that he can recover no more than he would have suffered if he had acted reasonably, because any further damages do not reasonably follow from the defendant's breach, the result is the same.*

In the ordinary course of litigation respecting wrongful dismissal, a plaintiff, in offering proof of damages, would lead evidence respecting the loss he claims to have suffered by reason of the dismissal. He may have obtained other employment at a lesser or greater remuneration than before and this fact would have a bearing on his damages. He may not have obtained other employment, and the question whether he has stood idly or unreasonably by, or has tried without success to obtain other employment would be part of the case on damages. If it is the defendant's position that the plaintiff could reasonably have avoided some part of the loss claimed, it is for the defendant to carry the burden of that issue, subject to the defendant being content to allow the matter to be disposed of on the trial judge's assessment of the plaintiff's evidence on avoidable consequences. This is the way I read what is said on the matter in such leading textbooks on the subject as Cheshire and Fifoot's, Law of Contract, 8th ed. (1972), at p. 599, and Corbin, Contracts, vol. 5 (1964), at p. 248. The matter is put as follows in two passages from Williston on Contracts, vol. 11, 3rd ed. (1968), at pp. 302 and 312:

> *The rule of avoidable consequences here finds frequent application. The consequence of this injury is the failure of the employee to receive the pay which he was promised but, on the other hand, his time is left at his own disposal. If the employee unavoidably remains idle, the loss of his pay is actually suffered without deduction. If, however, the employee can obtain other employment, he can avoid part at least of these damages. Therefore, in an action by the employee against the employer for a wrongful discharge, a deduction of the net amount of what the employee earned, or what he might reasonably have earned in other employment of like nature, from what he would have received had there been no breach, furnishes the ordinary measure of damages.*
>
> ...
>
> *It seems to be the generally accepted rule that the burden of proof is upon the defendant to show that the plaintiff either found, or, by the exercise of proper industry in the search, could have procured other employment of an approximately similar kind reasonably adapted to his abilities, and that in absence of such proof the plaintiff is entitled to recover the salary fixed by the contract.*

> *Cheshire and Fifoot, supra, expressed the position more tersely as follows:*
>
> > *But the burden which lies on the defendant of proving that the plaintiff has failed in his duty of mitigation is by no means a light one, for this is a case where a party already in breach of contract demands positive action from one who is often innocent of blame.*

[152] The duty to mitigate applies equally to claims in tort, as well as in contract. Binnie J, for the majority, of the Supreme Court of Canada in *British Columbia v Canadian Forest Products Ltd*, [2004] 2 SCR 74, wrote at paragraphs 106 and 107:

> *106 The law requires a plaintiff to take reasonable steps to mitigate its loss. When mitigation yields a sum of money equal to or greater than the original loss, the plaintiff has made himself whole, and cannot claim further from the defendant. The argument is that the Crown, having successfully recouped its loss under the CVP "waterbed" effect, has no further claim. Hall J.A. accepted the application of the mitigation principle here, relying on the well-known formulation of the principle in British Westinghouse Electric and Manufacturing Co. v. Underground Electric Railways Co. of London, Ltd., [1912] A.C. 673 (H.L.). In that case, the plaintiff, having lost the use of its obsolete generating equipment by reason of a breach of contract, took immediate steps to purchase more efficient generators whereby "all loss was extinguished ... actually the respondents made a [page125] profit by the course they took" (p. 688). In these circumstances, Viscount Haldane observed, at pp. 690-91:*
>
> > *The subsequent transaction, if to be taken into account, must be one arising out of the consequences of the breach and in the ordinary course of business.*
> >
> > ...
> >
> > *The transaction was not res inter alios acta, but one in which the person whose contract was broken took a reasonable and prudent course quite naturally arising out of the circumstances in which he was placed by the breach.*

> *107 The British Westinghouse principle of mitigation has been extended to tort claims: Andros Springs v. World Beauty, [1970] P. 144 (C.A.); Bellingham v. Dhillon, [1973] Q.B. 304 (C.A.); 1874000 Nova Scotia Ltd. v. Adams (1997), 146 D.L.R. (4th) 466 (N.S.C.A.); and S. M. Waddams, The Law of Damages (4th ed. 2004), at para. 15.730. Waddams summarizes the effect of the mitigation cases, at para. 15.800:*
>
> > *These considerations suggest what seems to be a test often applied, that is, whether the plaintiff could, even in the absence of the wrong, have made the disputed profit. If so, it is treated as collateral. If not, it goes to reduce the plaintiff's loss.*
>
> *See also Karas v. Rowlett, [1944] S.C.R. 1; Cemco Electrical Manufacturing Co. v. Van Snellenberg, [1947] S.C.R. 121; Apeco of Canada, Ltd. v. Windmill Place, [1978] 2 S.C.R. 385; Asamera Oil Corp. v. Sea Oil & General Corp., [1979] 1 S.C.R. 633.*

[153] To the same effect is the decision of the Ontario Court of Appeal in *Turczinski v Dupont Heating & Air Conditioning*, [2004] OJ No. 4510, 246 DLR (4th) 95 (CA), where Feldman JA, for the Court, wrote at paragraphs 43 and 44:

> *43 [42] The trial judge was satisfied that the respondent should receive some compensation for the loss of rent and considered the issue to be whether the respondent had a duty to mitigate her damage by making the rooms habitable and available to rent. The trial judge viewed the respondent as a thin-skull plaintiff, applying the Supreme Court of Canada decision in Janiak v. Ippolito (1985), 16 D.L.R. (4th) 1. In that case, the plaintiff suffered a serious spinal injury in a motor vehicle accident. The plaintiff refused to have corrective surgery that had a 70 per cent chance of enabling him to resume his former employment. The issue was the extent of a tort victim's duty to mitigate his damages for loss of income.*
>
> *44 [43] The court held that if a tort victim has a pre-existing psychological infirmity that makes him incapable of making a decision regarding surgery, then he is a thin-skull plaintiff who does not bear the burden of his incapacity. Otherwise, a tort plaintiff is obliged to mitigate his or her damages by acting reasonably.*

[154] Onus has no role to play in assessing mitigation; the duty of the Court is to look at the evidence in the record and determine whether and when it was appropriate to mitigate the losses claimed. Pelletier JA, for the Federal Court of Appeal, clearly set out this principle in *Chopra v Canada (Attorney General)*, [2008] 2 FCR 393 (CA), at paragraphs 40 to 42:

> *40 That said, the discretion given to the Tribunal to award any or all of the losses suffered leaves it open to the Tribunal to impose a limit on losses caused by the discriminatory practice. A tribunal may well find that the principles underlying the doctrine of mitigation of losses [page415] in other contexts apply equally in the context of claims for lost wages under the Act. Society has an interest in promoting economic efficiency by requiring those who have suffered a loss to take steps to minimize that loss as it is not in the public interest to allow some members of society to maximize their loss at the expense of others, even if those others are the authors of the loss: see British Columbia v. Canadian Forest Products Ltd., [2004] 2 S.C.R. 74, at paragraph 184. Thus while a tribunal is not bound to apply the doctrine of mitigation, it is not prohibited from doing so in the exercise of its discretion to determine the amounts payable to a complainant.*
>
> *41 Dr. Chopra argues that if those principles are to be applied, then the Tribunal incorrectly placed the onus on him to prove it. The following passage is illustrative, in Dr. Chopra's view, of the Tribunal's error: "the Complainant must show that he took steps to improve his chances of successfully competing for an EX-level position and that he applied for such positions where the opportunity arose": see remedy decision, at paragraph 37.*
>
> *42 The question of onus is, with respect, a red herring. Where the evidentiary record allows the Tribunal to draw conclusions of fact which are supported by the evidence, the question of who had the onus of proving a given fact is immaterial. The question of onus only arises when it is necessary to decide who should bear the consequence of a gap in the evidentiary record such that the trier of fact cannot make a particular finding. "Onus has no role to play when all the evidence is in the record": see Red Deer College v. Michaels, [1976] 2 S.C.R. 324 [at pages 346-347] per de Grandpré J.*

[155] Therefore, in looking at the evidence in this case, it is clear that Apotex knew it could mitigate its losses by conducting tests using a Canadian reference standard. It did precisely that in respect of Apo-Zidovudine. As Dr. Sherman wrote to HPB on May 10, 1991 respecting Apo-Zidovudine (Exhibit 1, Tab 87):

> *We will also mitigate damages by commencing the repeat study and will seek to hold HPB liable, for both the cost of the study and damages from delay in review and approval.*

[156] In portions of Apotex's Examination for Discovery filed by the Defendant at trial, Dr. Sherman testified that it might have taken a few months and cost one to two hundred thousand dollars at the time to do a repeat study (Exhibit 16, Tab 3). In his examination in chief at trial, Dr. Sherman testified a repeat study would have taken six months, causing an eighteen month delay, assuming HPB issued an NOC one year after receiving the repeat study (Pages 95-95 of the Transcript). In accordance with the rule in *Browne v Dunn*, counsel for the Defendant put Dr. Sherman's statement in the Examination for Discovery to him at trial (Pages 344 to 346 of the Transcript):

> *Q. The answer is: "it might have taken a few months and cost one to $200,000 at the time."*
>
> *A. Yes.*
>
> *Q. So a few months -*
>
> *A. A few months is the lower - depends on the circumstances. If you found an outside lab that had already validated a method and could schedule it to do it immediately you could do it in a few months. I would say three to six months. More likely six, but it could be a few months.*
>
> *Q. Somewhere between a hundred to $200, 000?*

A. That was a guess. Depends where it's done. We can do bio studies in India for a hundred thousand and in North America they're usually closer to 500 thousand.

Q. Now. What about back then?

A. I'd say 3/400 thousand.

Q. Are you resiling from the evidence that you gave at your examination?

A. It depends on how difficult the analytic method is. I don't know whether this is a simple method of GC, GCMS. I can't say.

Q. You said a hundred to 200 thousand?

A. ***It might have taken a few months, cost a few hundred thousand at the time. This is going back - 200 thousand is probably a fair estimate but I don't know*** *[emphasis added]*

Q. You were only asked to estimate. That's fair enough. Thank you.

A. Yes. I notice above I was asked why it wasn't done and I gave the explanation. There was no reason.

Q. Which you've given in court today?

A. Yes, same answer.

Q. If I could ask you then to turn to - I think we can skip that.

A. Dr. Sherman, if you had capitulated and chosen to do the bioavailability study and you had done it in May of 1989 -

A. Yes.

Q. - when you first got that letter saying we need a Canadian bioavailability study -

A. Yes.

Q. - I put it to you that had you done that and you had undergone few months as you say of delay?

A. ***Three to six months, yes*** *[emphasis added].*

[157] Hence, the record shows that the cost of a repeat study using a Canadian reference standard for Apo-Trazadone would be about $200,000 to $300,000, and take some three to six months (Pages 344-345 of the Transcript). Presumably if all was satisfactory, an NOC would have been granted to Apotex in about one year after submitting said repeat study. This is what could have been done, the question is whether and when it would have been reasonable to do so.

[158] Apotex was persisting in its position that a non-Canadian reference product was logical and reasonable. It wanted to make a point. Ultimately, it did so, and received an NOC in February 1995. By the end of 1995, HPB published a comprehensive set of guidelines respecting the circumstances respecting the use of reference products.

[159] However, the Court should not view the question of damages and mitigation from the point of view of a party wanting to make a point. Here, we are dealing with economic circumstances, loss by one party, and payment out of the public purse by another. Damages here are not an award for winning a point, damages are to provide reasonable compensation for unavoidable loss. The reasonable person thinks in terms of economics, not principle.

[160] In the period from April 25, 1991 to July 31, 1991, Apotex wrote to HPB asserting that it was suffering damages and requesting that HPB accept Apotex's submissions based on a non-Canadian reference. On July 17, 1991, Apotex brought its second judicial review, requesting an Order that the Court review Apotex's submission based on the non-Canadian reference. On January 19, 1993, the Court gave an Order dismissing Apotex's request.

[161] I find that a reasonable person, thinking in terms of economics, would have taken steps to mitigate its damages by July 2, 1991, the date Apotex wrote to HPB advising that it would mitigate its damages for Apo-Zidovudine (Exhibit 1, Tab 102). While the taking of Court proceedings is fine from a point of principle, from a point of economics, mitigation, instead of or in addition to Court proceedings, is what a reasonable person would have done.

[162] In find that, as of July 2, 1991, Apotex should have retested its product using a Canadian reference standard, this would have taken three to six months. Had it done so, at a cost of $200,000 to $300,000, and assuming the tests were favourable, Apotex may have received its NOC in about fifteen to eighteen months from July 2, 1991, the date it commenced the repeat study, that is, about mid-November of 1992.

[163] Therefore, in assessing damage, the starting date should be, as I have determined, November 26, 1991, but the termination date should be mid November, 1992, that is, to fix a date, November 16, 1992, the date an NOC would have been received if steps to mitigate had been taken. Apotex should also recover the costs of testing against a Canadian reference product, which were estimated to be two to three hundred thousand dollars.

Punitive Damages

[164] Apotex has asked that the Court impose punitive damages against the Defendant.

[165] As Binnie J held for the majority in *Whiten v Pilot Insurance Co*, [2002] 1 SCR 595 at para 36, punitive damages are awarded in exceptional cases to punish a Defendant for malicious,

oppressive and highhanded misconduct that represents a marked departure from the ordinary standards of decent behaviour and thus offending the Court's sense of decency. Damages are intended to compensate the wronged party for its loss. By contrast, punitive damages would over-compensate the wronged party and should only be imposed where there has been wrongdoing to such an extent that punishment is warranted.

[166] Here, the Defendant is Her Majesty. The Crown has, for some time, been liable in tort and damages may be assessed against the Crown where appropriate. Punishable wrongdoing, however, is something done by agents or servants of the Crown. Imposing punitive damages against the Crown for the acts of its servants or agents requires at least some form of complicity or blameworthiness on the part of the Crown as employer (*Tshekalin v Brunette*, [2004] OJ No 2855 at para 90, 132 ACWS (3d) 608 (Sup Ct), citing MacGuigan JA's judgment for the Federal Court of Appeal in *Peeters v Canada*, [1993] FCJ No 1146 at para 20 (CA)). Similarly, in *Blackwater v Plint*, [2005] 3 SCR 3 at para 91, McLachlin CJ writing for the Court held that finding the Crown vicariously liable for punitive damages requires "reprehensible conduct specifically referable to the employer."

[167] In the present case, I do not find that the actions of the HPB personnel are sufficiently egregious so as to warrant an award of punitive damages against Her Majesty. I make this finding notwithstanding my finding of the Defendant's liability under the tort of misfeasance in public office, as Prothonotary Aalto found in *McMaster* at paragraph 66, "While the conduct causing the injury is unlawful it does not necessarily incur a punitive element."

Conclusions and Costs

[168] I have found that the Defendant is liable for damages to Apotex in tort, namely, misfeasance in public office and negligence to Apotex. These damages should have been mitigated by Apotex. As a result, damages should be calculated on the basis that Apotex should have been given its NOC as of November 26, 1991, and should have mitigated its damages on July 2, 1991, which would have resulted in an NOC being given to Apotex as of November 16, 1992. Apotex should also recover the reasonable costs of testing against a Canadian reference product, estimated to be in the range of two to three hundred thousand dollars.

[169] A reference or trial as to the extent of damages has been Ordered on July 31, 2003. A trial would be more expedient. Either or both parties should apply within a reasonable time to this Court with a schedule as to how matters should proceed in that regard.

[170] Counsel have asked that I reserve on costs pending further submissions having regard to these Reasons. I expect to receive those submissions in writing within the next fifteen days.

"Roger T. Hughes"
Judge

Ottawa, Ontario
November 18, 2014

SCHEDULE A

Date	Document Type	Summary of Document	Source
February 1981	Bureau of Human Prescription Drugs, Drugs Directorate, Health Protection Branch: *Guidelines for New Drug Product Requirements*:	The Guideline provided "the bioavailability of the new drug product is compared to that of an acceptable standard…The manufacturer of a new generic drug product must provide evidence that the active ingredient(s) in his product are chemically equivalent to those an acceptable standard [emphasis in original]."	Exhibit 1, Tab 2.
November 9, 1981	Letter to S Szabolcs, Scientific Director of Apotex from M.I. Inamirovska, M.D.	HPB found Apotex's NDS submission for Apo-Spiroside Tablets incomplete in complying with the requirements of Section C.08.002 of the *Food and Drug Regulations*. They advised Apotex provide for review an additional bioavailability study using Apotex's product and a product marketed in Canada.	Ex 1, Tab 3.
April 22, 1982	Letter from Dr. Ian W.D. Henderson, M.D. Director of the Bureau of Human Prescription Drugs, HPB to Ms. Szabolcs.	HPB found Apotex's NDS submission for Apo-Spiroside Tablets incomplete because the Canadian and American formulations "are not identical". HPB recommended "the study be carried out using Canadian Aldactaride as the reference product and Apo-Spiroside. The latter should have the identical composition and manufacturing procedure as that which you intend to market in Canada."	Ex 1, Tab 4.
March 29, 1983	Unsigned letter from Bristol-Myers Pharmaceutical Group to Dr. Henderson.	Regarding Bristol-Myers's approved NDS for Desyrel they submitted "15-day" received from their affiliate Mead Johnson and Company in the United States for Desyrel.	Ex 1, Tab 6.
April 28, 1983	Unsigned letter from Bristol-Myers to Dr. Henderson.	Bristol-Myers enclosed copies of several documents relating to the adverse reactions to Desyrel reported to Mead Johnson, as well as case histories and the latest Desyrel package being used in the U.S.	Ex 1, Tab 7.
March 22, 1984	Unsigned HPB Memorandum to	This is in relation to Forest Laboratories, Inc.'s Theophylline and comments that "Theo Dur	Ex 1, Tab 8.

	Dr. Henderson	tablets are an acceptable reference standard. Comparability of U.S. vs. Canadian Theo Dur products was not provided."	
July 13, 1987	Letter to Ms. Szabolcs for Apo-Vet Inc from D.A. Landry chief of Antimicrobial Drugs Division in HPB.	Regarding Apo-Vet's Veterinary NDS for Amoxi tablets, 100 mg: "the bioequivalency trial which used AMOXI-TABS, manufactured and sold in the United States by Beecham Laboratories, has no been considered eligible for review."	Ex 1, Tab 10.
December 22, 1987	Letter from Leo P. Fleming of Bristol-Myers to Dr. A Rein.	Regarding Canadian Desyrel: "The product sold by Mead Johnson in the United States and that sold by ourselves under the trade name <u>are identical</u>" [emphasis in original].	Ex 1, Tab 24.
January 25, 1988	Letter delivered via courier from Jim Lipa of Apotex to Dr. Henderson	**Filing of Apotex's NDS for Apo-Trazad** 50 and 100 mg tablets. According to Dr. Sherman's testimony, Apotex also included the December 22, 1987 Bristol-Myers letter, as well as the literature on the U.S. product with the NDS.	Ex 1, Tab 13.
April 25, 1988	Letter from Solange Ducharme, Submission Control Division of HPB to Mr. Lipa of Apotex.	HPB confirms receipt of Apotex's NDS for Apo-Trazad and would commence review of said NDS "as soon as possible".	Ex 1, Tab 16.
April 25, 1988	Screening review from Peter Jeffs, Chief of Pharmaceutical Evaluation Division of HPB to Dr. T. DaSilva, Chief of Central Nervous System Division of HPB.	Apo-Trazad was "NOT CLEARED."	Ex 1, Tab 17.
January 20, 1989	Memorandum from Dr. Gordon E. Johnson, Director of the Bureau of Human Prescription Drugs, HPB, to Dr. E Somers, Director General of the Drugs	After reviewing Apotex's NDS, Dr. Johnson stated "it is not illogical to conclude that the bioavailability study done on the Barr and Mead Johnson products is applicable to the Apotex and Bristol products marketed in Canada" and was inclined to accept Apotex's argument "on the basis of science alone." However, in recognition that this could be a precedent setting case, he suggested contacting Bruce Rowsell to discuss the NDS before coming to a decision on	Ex 1, Tab 21.

	Directorate, HPB.	the same.	
February 8, 1989	HPB Memorandum from Mr. Rowsell, Director of the Bureau of Pharmaceutical Surveillance, Drugs Directorate to Dr. Somers.	HPB should only consider the foreign reference product as suitable if it is "identical to that of the Canadian source." He recommended that "requirements for a comparative bioavailability study against the innovative product marketed in Canada not be waived on the basis of a third party letter from Bristol on Desyrel. This again emphasizes the need for clear guidelines to express our requirements." Regarding the December 22, 1987 letter: "should such a letter be accepted as evidence of identical products since the capability of the letter's author to render such a judgement would be based solely on the job title in the letter and since the authenticity of the letter has not (can not?) been verified?"	Ex 1, Tab 22.
April 3, 1989	Letter from Dr. Sherman to Dr. Johnson.	Apotex was developing indomethacin slow-release capsules 75 mg for sale in Canada and in the United States. Dr. Sherman requested that HPB advise if they would allow the U.S. Indocin-SR as an acceptable reference product. He stated that the Canadian Indocid-SR and the U.S. Indocin-SR "are apparently identical and known to have identical pharmacokinetic profiles." He also referred to the above-referenced March 22, 1984 memo as an example of a situation "where HPB has deemed the U.S. product to be a satisfactory reference, where the U.S. and Canadian reference product were known to have the same profiles and where it would be unreasonable to request that studies be repeated Using the Canadian reference."	Ex 1, Tab 29.
May 1, 1989	Letter from Dr. DaSilva to Ms. Szabols.	Dr. DaSilva advised that the NDS for Apo-Trazad did not comply with section c.08.002 of the *Food and Drug Regulations*: "As you are aware" the NDS should include "bioavailability studies comparing your proposed product with the standard trazodone product marketed in Canada, in order to determine their bioequivalence."	Ex 1, Tab 23.
May 10, 1989	Letter from Ms. Szabolcs to Dr. DaSilva with enclosures from March 29, 1983,	Ms. Szabolcs advised that the manufacturer already confirmed in writing "that the Canadian and U.S. brands are identical". She cited the above-referenced example Theophylline wherein HPB "accepted the U.S. brand as a	Ex 1, Tab 24.

	April 28, 1983, March 22, 1984 and December 22, 1987, all included above.	reference, when it was reasonable to believe that the U.S. and Canadian brands were the same."	
June 23, 1989	Memo from Dr. Somers to the Drugs Directorate Management Committee.	NDS's for generic drugs should contain comparative bioavailability studies that "should be performed by the use of the corresponding currently marketed Canadian drug formulation as the essential reference standard."	Ex 1, Tab 28.
June 29, 1989	Letter from Dr. Sherman to Dr. Somers.	Apotex transmitted a copy of the April 3, 1989 letter which they received no reply in order to emphasize "As discussed we believe there are circumstances in which it would be unreasonable to insist on Canadian sourcing of the reference. Such circumstances would include a case in which <u>all</u> of the following apply [emphasis in original]: 1. The proposed source of the reference product is the major market of the originator. 2. The originator's product is apparently the same in both countries. 3. The originator's publications confirm that products to be the same, or at least there is no basis to suggest that there is a difference. 4. The originator has obtained its own Canadian approval on the basis of data generated on the product as sold in the major market. 5. The published literature submitted by the generic manufacturer to demonstrate safety and efficacy is or appears to be based on the product as sold in the major market. 6. The generic manufacturer proposes to develop its product for sale in both countries and would be unreasonably burdened by the need to do separate studies for each country." 7. In later communications to HPB set out below, Dr. Sherman often discusses and elaborates on these circumstances.	Ex 1, Tab 29.
June 30, 1989	Memo from Mary Carman	"The attached policy statement", of June 23, 1989 "was recently developed." She	Ex 1, Tab 29.

	(Kasparak), Acting Chief of Drug Regulatory Affairs Division, Drugs Directorate of HPB to Dr. Johnson with enclosures from April 3, 1989, June 23, 1989 and June 29, 1989, included above	recommended HPB review the points Dr. Sherman raised in his June 29, 1989 letter to determine whether to amend said policy statement. She requested providing written comments to Dr. Sherman's points by July 21, 1989.	
July 10, 1989	Memo from Dr. Johnson to Ms. Carman (Kasparak), following up from the June 30, 1989 communication.	HPB should not "accept studies conducted outside Canada against the innovator's brand as sold in a major market area if the innovator has manufacturing capabilities in Canada and formulates his product in our country." The Canadian reference product must remain "our 'gold standard' against which imitators should make their comparisons."	Ex 1, Tab 30.
August 18, 1989	Memo from DaSilva to Peter Jeffs, Chief of Pharmaceutical Evaluation Division of HPB, cc'ing Dr. Johnson.	He discussed the Apo-trazadone submission with Dr. Johnson and Mr. Rowsell. He informed Apotex on May 1, 1989 that HPB requires bioavailability studies comparing Apo-Trazadone product with a product marketed in Canada rather than one in the U.S. He then stated to the recipients of the letter that HPB provided a policy instruction that a foreign product could be a suitable reference product if the applicant could show the "Canadian source" identical to the foreign product. However, if HPB knows of any precedent of accepting a foreign product rather than a Canadian product "we would be duty bound to bring this to the attention of management before proceeding any further."	Ex 1, Tab 31.
August 24, 1989	Letter to Dr. Sherman from Dr. Somers responding to Dr. Sherman's June 29, 1989 letter.	Dr. Somers emphasized the importance of the requirement for Canadian sourcing for the purpose of establishing safety and efficacy. "When the reference product cannot be conclusively proven to be identical to that marketed in Canada, parity of performance with a product known to the Branch can not be assumed." Instead of comparative bioavailability studies, the manufacturer could conduct original clinical research to establish	Ex 1, Tab 32.

		safety and efficacy of the test product. He noted the conditions Dr. Sherman proposed "to forego Canadian sourcing of the reference product do not conclusively prove that a non-Canadian reference product is identical to the Canadian version."	
August 24, 1989	Memo to Dr. DaSilva from Mr. Jeffs, following up to the August 18, 1989 memorandum.	He knows of precedents of where HPB accepted a foreign product as the standard in a comparative bioavailability study "simply because the question of the source was never asked." Although Dr. Johnson and Dr. Somers know this, Dr. DaSilva advised that Dr. Somer's believes that those precedents "should not affect our decision to implement a current policy." Dr. DaSilva recommended simply telling Apotex that the current Drugs Directorate policy states "that comparative bioavailability studies should be performed Using the currently marketed Canadian product as the reference standard.	Ex 1, Tab 33.
August 29, 1989	Memo from Dr. DaSilva to Dr. Johnson, cc'ing Mr. Jeffs, attaching the January 20, 1989, February 8, 1989, June 23, 1989, August 18, 1989 communications and the August 24, 1989 memo, included above.	He summarizes the activity related to these communications, and discussion he had with Mr. Jeffs and concludes "Since I am unable to follow the previously suggested course of action, I would appreciate your guidance as to how we should proceed with regards to this Submission."	Ex 1, Tab 34.
September 27, 1989	Memorandum from Eric D. Ormsby from the Bureau of Drug Research, HPB to Dr. C. Peterson, Bureau of Human Prescription Drugs, HPB	He reanalyzed the Trazodone comparative bioavailability study of single oral 100 mg doses of Barr and Mead Johnson 100 mg trazodone HC1 tablets which Apotex submitted and found "From these results it would seem that the two formulations have similar rates and extents of bioavailability."	Ex 1, Tab 36.
November 30, 1989	Letter to Dr. Sherman from Dr. K.J Michalko, Chief of the Division of	Based on the policy statement HPB cannot confirm that the U.S. Indocin-SR will be an acceptable reference product for comparative bioavailability studies against Apotex slow-release capsules. "Central to the policy is the	Ex 1, Tab 38.

	Biopharmaceutical Evaluation from HPB, copying Mr. Rowsell. The letter included a copy of the June 23, 1989 policy statement.	difficulty for manufacturers to conclusively prove the equivalency of another manufacturer's U.S. and Canadian formulations coupled with instances where different formulations have been utilized for the same brand name in Canada and the U.S.A."	
December 18, 1989	Memo from Dr. Michalko to Mr. Jeffs, cc'ing Dr. Wayne Nitchuk of HPB. It attached the letter of May 10, 1989.	Based on the third party letter HPB needs to address (1) "what statement best summarizes current policy regarding the acceptance of certified data or information which may not be verifiable by the Branch except by consulting another manufacturer's submission?", and (2) should they still require "a Trazodone reference product which was obtained from the Canadian market?"	Ex 1, Tab 39.
February 1, 1990	Letter to Ms. Szabolcs from Dr. Michalko following up to Ms. Szabolcs letter of May 10, 1989.	They allege that Ms. Szabolcs's requested HPB waive the "normal requirement" for Using a Canadian reference product. They found the third party letter Apotex provided "is not acceptable evidence to establish that Apo-Trazad need not be compared to Desyrel tablets as obtained from the Canadian market." Any attempt by HPB to inquire to the manufacturer in the U.S. "would undoubtedly be fruitless as the manufacturer is under no obligation to reply." Hence Apotex must Use a product from the Canadian market "unless incontrovertible and verifiable evidence can be provided to establish that the product in a foreign market is identical in all respects to the Canadian product."	Ex 1, Tab 40.
March 8, 1990	Lengthy letter from Dr. Sherman to Dr. Somers in reply to Dr. Michalko's letter of February 1, 1990	HPB should consider Apotex's NDS based on the study Apotex submitted. He provided several reasons to argue HPB illogically required Apotex provide a comparative bioavailability study based on tablets purchased in the Canadian market rather than in the U.S. market. For one of these reasons he submitted that "In this case the two references are the same…we have provided a letter from the originator which unequivocally confirms that Canadian and U.S. Desyrel are identical [emphasis in original]." He also cited three cases where HPB accepted the Use of a	Ex 1, Tab 41.

		reference purchased in the foreign market of the originator: 1. Amoxi tablets of Apo-Vet Inc. for which AMOXI-TABS sold by Beecham in the U.S. was the reference product; 2. Theophylline slow release tablets of both Apotex and Forest Laboratories, for which the Bureau accepted THEO-DUR tablets purchased in the U.S. as a reference; and 3. Tamoxifen tablet of both Apotex and Rhone-Poulenc for which HPB accepted NALVADEX tablets purchased in Europe as the reference. "Undoubtedly there are other such cases." Dr. Sherman requested a prompt reply since any delay in approval on the basis of requiring a Canadian reference would severely prejudice Apotex.	
March 27, 1990	Memo from Dr. Michalko to Dr. Somers, cc'ing Mr. Rowsell.	"Dr. Sherman is correct in noting that the policy has not been invariably maintained by BHPD. Additionally, he is correct in his claim that your policy statement of June 23, 1989, which reaffirmed this matter, was not publicly released."	Ex 1, Tab 43.
April 4, 1990	Letter from Dr. Somers to Dr. Sherman in response to Dr. Sherman's letter of March 8, 1990	He stated that HPB already advised Apotex of a long-standing policy of requiring a Canadian reference product for comparative bioavailability studies in the 1981 correspondence to Apotex on Apo-Spirozide. He emphasized HPB would maintain this requirement for Apo-Trazad.	Ex 1, Tab 44.
April 10, 1990	Letter from Dr. Sherman to Dr. Somers responding to the April 4, 1990 letter.	He stated Dr. Somers's letter was inaccurate and advised that "unless you are prepared to consider our submission on its merits, we will have no alternative but to apply to the Federal Court for an order requiring you to carry out your statutory obligation."	Ex 1, Tab 45.
May 1, 1990	Letter from Dr. Somers to Dr. Sherman, following up to the April 10, 1990 letter.	HPB long required Using a currently marketed Canadian drug formulation and they communicated this requirement to Apotex as early as December 11, 1981 and emphasized that they consider the policy as "fair, scientifically credible and consistent with good international practice." However, "As with all procedures we are prepared to consider	Ex 1, Tab 46.

		exceptions based on their scientific merits, for we are not inflexible."	
May 8, 1990	Letter from Dr. Sherman to Dr. Somers responding to the May 1, 1990 letter.	He disputes the accuracy of that letter, stating that HPB established this policy only after Apotex's enquiry of April 3, 1989. Moreover, subsequent to the letter of December 11, 1981, Dr. Henderson stated at a meeting on January 5, 1982 "that the U.S. reference was not necessarily unacceptable. The U.S. reference was ultimately not accepted only because in that case the U.S. and Canadian references were not the same. This was explained in Dr. Henderson's letter of April 22, 1982." Dr. Sherman then noted that Using foreign reference products is a growing trend and that Apotex is merely asking that HPB consider the NDS "on the scientific merits, as you say you are prepared to do." Finally he refers to a meeting at Dr. Somers's office of November 1989 in relation to Apo-Salvent Solution where HPB advised "that a letter from the originator confirming the Canadian and foreign reference brands to be the same would be accepted as confirming evidence."	Ex 1, Tab 47.
May 16, 1990	Letter from Dr. Somers to Dr. Sherman, following up to the May 8, 1990 letter.	"Full evaluation of Apo-Trazad will commence based on its date of receipt." He reasserted the "requirement for a study-utilizing a reference product from the Canadian market."	Ex 1, Tab 48.
July 10, 1990	Letter from Dr. Sherman to Dr. Somers in response to the May 15, 1990 letter.	He once again disagreed with Dr. Somers's position regarding the requirement for the Canadian reference product. He provided a draft of the Notice of Motion and Affidavit intended for filing in the Federal Court and stated if they did not have confirmation within two weeks "that the reference need not necessarily be purchased in Canada, we will proceed with filing and service of the legal documents."	Ex 1, Tab 50.
July 17, 1990	Letter from Dr. Somers to Dr. Sherman following up to the letter of July	HPB would adhere to "the required Use of a referenced product from the Canadian market in comparative bioavailability studies for generic drugs."	Ex 1, Tab 51.

	10, 1990.		
July 30, 1990	Dr. Sherman's affirmed affidavit for the purpose of Judicial Review I.	Amongst other things, Dr. Sherman stated "Since the Apotex submission included published literature supporting the safety and efficacy of the original brand, and since the literature related to the American product, it was not logical to require a bioavailability study comparing Apo-Trazad with the Canadian original brand…In any case, the evidence given demonstrated that the original brands in the United States and Canada were the same." Dr. Sherman also referred to Amoxi tablets, Theophylline slow-release tablets and Tamoxifen tablets as examples of circumstances where "the practice of H.P.B. has in fact been to accept a bioavailability study Using as a reference brand the original brand sold in the originator's major market."	Ex 2, Tab 2.
August 13, 1990	**Judicial Review I: Notice of Motion filed at the Federal Court of Canada, Trial Division**, signed by H.B. Radomski, lawyer for Apotex (T-2276-90).	Apotex requested the Court make an order directing the Minister of National Health and Welfare to review Apotex's NDS in respect of Apo-Trazad to determine whether, "and more particularly, the comparative bioavailability study, literature review and other data contained therein, adequately establish the safety and effectiveness of Apo-Trazad for Use as a drug in Canada without regard to a condition precedent to review that the reference product tested in the comparative bioavailability study be purchased in Canada."	Ex 2, Tab 1.
August, 1990	Expert Advisory Committee on Bioavailability of the HPB's *Report on Bioavailability of Oral Dosage Formulations of Drugs Used for Systemic Effects: Drugs with Uncomplicated Characteristics*.	Dr. Michael Spino, an Associate Professor of the Faculty of Pharmacy at the University of Toronto was a member of this Advisory Committee. The Report provides "In bioequivalence studies, the reference product must be marketed in Canada by the innovator, his licensee, or if there is no recognized innovator, the market leader."	Ex 1, Tab 52.
September 27, 1990	Mr. Rowsell's sworn affidavit for the purpose of Judicial Review I.	Regarding the existence of a policy requiring the Use of a Canadian Reference Product: • "The Health Protection branch required for many years that a comparative	Ex 2, Tab 3.

		bioavailability study that is submitted under subsection c.08.002(2) of the Food and Drug Regulations to establish the safety and efficacy of a new drug to be marketed for sale in Canada or a drug product that has been confirmed as identical to a drug product marketed for sale in Canada… • This requirement has been in force for many years and was re-affirmed in a policy statement in June of 1989. • Apotex has been aware of this policy since at least 1981." Mr. Rowsell then addressed the three circumstances Dr. Sherman raised that HPB departed from that policy • Amoxi tablets: "the comparative bioavailability study submitted by Apo-Vet Inc. in respect of their Amoxi tablets was in reference to a drug product that was identical to a drug product marketed for sale in Canada...The Health Protection Branch confirmed by telephone with the manufacturer that the drug products were identical." • Theophylline: Based on the information Mr. Jeffs provided, Mr. Rowsell stated "It was known from public literature that the reference product was manufactured uniquely at one foreign facility and marketed worldwide by licensed distributors." • Tamoxifin: Based on the information Mr. Jeff provided, Mr. Rowsell believed "the comparative bioavailability study submitted by Apotex Inc. in respect to their tamoxifen tablets was in reference to a drug product identical to a drug product marketed for sale in Canada."	
October 9, 1990	Dr. Sherman's affirmed supplemental affidavit which responds to Mr. Rowsell's affidavit for the	"[T]he assertion that there was a new policy in force is incorrect…on June 26, 1989, I spoke to Dr. Somers about the Apo-Tamox submission and the refusal to that point of the H.P.B to approve same on the basis that the reference was not a Canadian reference. Dr. Somers agreed in that conversation that there was a need on the	Ex 2, Tab 4.

	purpose of Judicial Review I.	part of the H.P.B to remain flexible and to review each submission on its merits without adherence to a rigid policy." In response to the allegation that HPB advised Apotex of a policy of requiring a Canadian reference product since 1981, Dr. Sherman stated "It is true that Dr. Znamirowska's letter" of November 9, 1981 "in the case of Apo-Spirozide has been cited as one of her concerns that 'the standard Used in this study is not available in Canada'. However, at a meeting subsequent tot hat letter held on December 11, 1981, Dr. I. Henderson…acknowledged that a reference product in the U.S. was satisfactory. The approval of Apo-Spirozide was subsequently refUsed only on the basis that the Canadian references were not the same, failing which the American reference would have been acceptable."	
November 2, 1990	Letter from Dr. R.G. McKeag of Apotex to Dr. Sherman, enclosing FTIR spectra data.	Dr. McKeag analyzed the FTIR data of 50 mg and 100 mg U.S. Desyrel against 50 mg and 100 mg Canadian Desyrel: "Fourier-Transform infrared analysis of the whole tablet material revealed that qualitatively, the Canadian and American formulations are absolutely identical. Quantitatively, the Canadian and American formulations were, within experimental error, virtually identical [emphasis in original]…Based upon this data, my conclusion is that the respective U.S.A. and Canadian Desyrel formulations are identical."	Ex 1, Tab 53.
November 5, 1990	**Settlement Meeting**: Handwritten note from Dr. Sherman to Mr. Rowsell which enclosed the November 2, 1990 information.	"Please add the following to our file as additional evidence of the equivalence of Canadian and U.S. Desyrel."	Ex 1, Tab 53.
November 6, 1990	HPB DBE Tracking System.	Assigns Dr. Cheriyan to review handwritten note of November 5, 1990 with the attached November 2, 1990 "FT-IR dissolution physical size + appearance comparison to establish that Canadian & U.S. products identical."	Ex 1, Tab 55.
November 13, 1990	Without prejudice fax to Mr.	"As discussed during our meeting in Ottawa on November 5, 1990, to settle the litigation	Ex 1, Tab 57.

	Radomski from Marlene L. Thomas, Senior Counsel for the Department of Justice, cc'ing Stuart Archibald, Counsel for Health & Welfare. Legal Services.	ongoing in the Federal Court, Trial Division and commenced by your Notice of Motion dated August 13, 1990, we are prepared to provide the following statement with regard to the subject matter of that litigation… • the review of your Apo-Trazad new drug submission is continuing and has not been completed for the purposes of section C.08.004 of the Food and Drug Regulations. If there are any deficiencies, they will be identified upon completion of the examination. • Any existing and further data provided by Apotex to establish Apo-Trazad is equivalent to a drug product currently sold in Canada will be considered. For the purposes of a comparative bioavailability study, the Health Protection Branch is prepared to consider scientific evidence to establish chemical and therapeutic equivalency between Canadian and non-Canadian reference standards. • Your client would withdraw the application to which we would consent without costs [bullet points added]."	
November 19, 1990	Document from Bruce Flann, Bureau of Drug Research to Michael Ward, Drug Manufacturing Specialist, Submission Control Division, Bureau of Pharmaceutical Surveillance, HPB.	This document included the raw data on Apo-Trazad with comments which Mr. Ward would review.	Ex 1, Tab 58.
November 26, 1990	**Settlement Agreement**: Letter from Ms. Thomas to Mr. Radomski, cc'ing Stuart Archibald.	"This letter confirms the agreement reached between the parties and counsel as to the settlement of this action, culminating in its withdrawal without costs before Jerome, A.C.J. in Motions Court of the Federal Court, Trial Division in Toronto on November 19, 1990. The	Ex 1, Tab 60

		Respondents hereby provide the following statement with respect to the subject matter of the litigation: • Further to recent discussions, this confirms that the review of your Apo-Trazad new drug submission is continuing and has not been completed for the purposes of section C.08.004 of the Food and Drug Regulations. If there are any deficiencies, they will be identified upon completion of the examination. • Any existing and further data provided by Apotex to establish that Apo-Trazad is chemically and therapeutically equivalent to a drug product sold in Canada will be considered. For the purposes of a comparative bioavailability study, the Health Protection Branch is prepared to consider evidence to establish equivalency between Canadian and non-Canadian reference standards [emphasis in original].	
December 6, 1990	Letter from Ms. Thomas to Mr. Radomski, cc'ing Mr. Archibald.	She confirmed that the parties agreed to settle the litigation and HPB officials have and will continue to conduct themselves "according to the terms of the agreement."	Ex 1, Tab 61.
December 6, 1990	Letter from Mr. Rowsell to Dr. Sherman.	The chemistry and manufacturing portions of the review for Trazodone is underway: "As our evaluation of the data you have submitted to establish that the Canadian and foreign reference products are identical is not yet completed, the safety and efficacy portion of the Trazodone submission is inactive [emphasis in original]."	Ex 1, Tab 62.
December 12, 1990.	Memo from Ukken Cheriyan a Chemistry Specialist in the Bureau of Pharmaceutical Surveillance to Dr. Wayne Nitchuk, Acting Head, Bureau of	After reviewing the data Apotex submitted on the testing of Canadian and U.S. Desyrel formulations he found that "Contrary to the company's claim, the information provided does not unambiguously prove that the two formulations are identical and I recommend that Apotex be advised accordingly." The memo then analyzed the FTIR spectra data and found that "Although the FTIR spectra of the two formulations are almost identical, the	Ex 1, Tab 63.

	Pharmaceutical Surveillance, HPB.	conclusion that the two formulations are qualitatively and quantitatively identical is scientifically untenable. In the IR spectra of complex mixtures, absorptions due to minor components are very often masked by those due to major components. Therefore, the presence of a minor component exclusively in one formulation cannot be ruled out." Mr. Ward added a handwritten comment on the memo dated December 11, 1990: "I agree with Dr. Cheryian's comments and overall conclusion."	
December 13, 1990	Letter from Mr. Radomski to Ms. Thomas in response to the letter of December 6, 1990.	He found Mr. Rowsell's Use of the term identical "disturbing" in view of the settlement agreement. He asked for her assistance "in ensuring that there is no misunderstanding as to the implementation of the settlement."	Ex 1, Tab 64.
December 14, 1990	Letter from Ms. Thomas to Mr. Radomski in response to the December 13, 1990 letter.	She advised that she is requesting Mr. Archibald to inquire on the point Mr. Radomski raised.	Ex 1, Tab 65.
December 17, 1990	Letter from Dr. Sherman to Mr. Rowsell in response to the December 6, 1990 letter.	Contrary to the December 6, 1990 letter, the parties settled the litigation "upon agreement by HPB that the reference need not be established to be identical, but that there need only be evidence that they are equivalent…As you are aware, HPB has accepted references purchased outside of Canada for other products, including tamoxifen, amoxicillin and theophylline." Since Apotex provided stronger evidence of equivalence than those cases "we believe that compliance with the settlement agreement compels a conclusion that the U.S. reference is acceptable in this case."	Ex 1, Tab 67.
December 18, 1990	Memo from Dr. Nitchuk to Mr. Rowsell.	Dr. Nitchuk forwarded Dr. Sherman's December 17, 1990 letter to Mr. Rowsell.	Ex 1, Tab 68.
December 20, 1990	Letter from Dr. Nitchuk to Dr. Sherman.	Dr. Nitchuk advised that HPB did not consider the submitted information "sufficient to establish equivalency of the Canadian and non-Canadian reference standard." HPB remains prepared to consider further data that Apotex would provide to establish Apo-Trazad is	Ex 1, Tab 69.

		chemically and therapeutically equivalent to a drug product sold in Canada. He noted direct confirmation from the manufacturer of the non-Canadian standard or a comparative bioavailability study that utilizes Desyrel tablets obtained from the Canadian market "would clearly satisfy the requirement of the Food and Drug Regulations."	
December 21, 1990	Letter from Dr. Sherman to Mr. Rowsell in response to Dr. Nichuk's December 20, 1990.	"As discussed yesterday, we believe that Dr. Nitchuk's letter of December 20, 1990 is inconsistent with the settlement agreement." He stated Dr. Nitchuk's position "is the same position as taken by HPB prior to the settlement agreement. A settlement agreement implies that there was movement by each party. Otherwise there was no consideration given by one of the parties for the agreement."	Ex 1, Tab 70.
December 27, 1990	Letter from Mr. Radomski to Mr. Archibald, cc'ing Ms. Thomas in response to Dr. Nitchuk's December 20, 1990 letter.	"Unfortunately, it appears that matters are not proceeding as was intended pursuant to the terms of the settlement…the essence of the settlement was to make it clear that 'identicality' was not a requirement, but that manufacturers such as Apotex needed to provide adequate evidence to establish the safety and efficacy of the submitted product", by demonstrating equivalency between a Canadian reference brand, known to be safe and effective, and a non-Canadian reference brand. Substantial evidence exists "to establish that Apo-Trazad is equivalent to the foreign reference brand…and that the latter is equivalent to the Canadian reference brand.'" He concludes by requesting assistance in ensuring that HPB gives appropriate consideration to Apotex's submission.	Ex 1, Tab 71.
January, 1991	HPB: *Therapeutic Products Programme Guideline: Preparation of Human New Drug Submissions*, Published by authority of the Minister of Health.	Introduction: "This guideline is not intended to be exhaustive or inflexible. Within the framework provided, appropriate adaptation may be made according to the type of drug product and the data available." Bioavailability:	Ex 9.

January 29, 1991	Letter from Dr. Nitchuk to Dr. Sherman.	"The chemistry and manufacturing portions" for Apo-Trazad "are under review…the safety efficacy review status is inactive." • "Human New Drug Submissions for 'generic' drug products should contain appropriate, adequate, and validated data from comparative bioavailability studies. • The comparative studies should Use the corresponding Canadian innovator drug product as the reference standard."	Ex 1, Tab 72.
February 4, 1991	Letter from Dr. Sherman to Mr. Rowsell in response to the January 29, 1991 letter.	"Dr. Nitchuk does not appear to be aware of the settlement…or your statement to me that the safety and efficacy review would now proceed." He then requested confirmation that the review would proceed promptly.	Ex 1, Tab 73.
February 20, 1991	Letter from Dr. Nitchuk to Dr. Sherman.	He advised that HPB scheduled the final review for the chemistry and manufacturing portions of the Apo-Trazadone submission for February 26, 1991 "Comments should be forthcoming within two days of the review being completed."	Ex 1, Tab 74.
February 26, 1991	Memo from Arvin Naperstkow a Chemist from the Bureau of Pharmaceutical Surveillance, HPB to Dr. Nitchuk.	This is a report on the chemistry and manufacturing of Apo-Trazadone. It concluded "the New Drug Submission is not recommended for clearance under section C.08.002 with respect to chemistry and manufacturing. Apotex Inc must address the following concerns before achieving compliance."	Ex 1, Tab 75.
February 28, 1991	Memo to Dr. Nitchuk signed by Bruce Flann, Mr. Naperskow, Mr. Ward and V Caron, it referred to Mr. Naperskow's report of February 26, 1991 and Mr. Ward's report of February 27, 1991	It concluded that the NDS for Apo-Trazad did not meet the requirements of C.08.002 of the Regulations "insofar as the chemistry, manufacturing, and product labelling portions are concerned." It recommended forwarding comments to the manufacturer which included the deficiency concerns of Mr. Naperstkow's memo, for example: 1. "Comments concerning deficiencies in the Product Master file for Trazodone hydrochloride has been forwarded directly to Farmos Group Ltd." 2. Confirm that reference products Used in the comparative dissolution study reported are "from the Canadian market." 3. "Your attention is drawn to the dissolution test in the proposed	Ex 1, Tab 76.

		monograph for Trazodone tablets…In the absence of a demonstrated in-vitro/in-vivo correlation the choice of medium (and other dissolution parameters) should normally be based upon the demonstrated or anticipated ability of the test to detect formulation and manufacturing changes."	
February 28, 1991	Report from Mr. Ward to Dr. Nitchuk, it included attachments related to the specifications of Trazodone, comparative dissolution rates of Trazodone, and documents related to labelling.	The report pertained to the manufacturing and relevant labelling portions of the Apo-Trazad submission. It concluded that the manufacturing and labelling aspects of the NDS failed to comply with C.08.002 of the Regulations. Mr. Ward noted "Curiously, in the additional information provided with Dr. Sherman's C/L of November 5, 1990…Apotex declares that 'all lots [of U.S. and Canadian sourced DESYREL examined] are at least 95% dissolved within 15 minutes.' Actual results and dissolution conditions were not described."	Ex 1, Tab 77.
March 8, 1991	Letter of Non-Compliance from Dr. Somers to Mr. John Hems, Manager of Product Development Administration at Apotex.	Pursuant to section C.08.004 of the *Food and Drug Regulations* the NDS does not comply with the requirements of section C.08.002 of the *Food and Drug Regulations*. "Consideration should be given to the following comments", it then provided the following two comments that did not appear in Mr. Naperskow's memo of February 26, 1991 or February 28, 1991: 1. This submission has failed to establish the safety and efficacy of Apo-Trazad Tablets in comparison to a <u>Canadian reference standard</u>. 2. The comparative bioavailability study is also deficient in that the test product is not from a batch intended for <u>sale on the Canadian market</u> [emphasis in original]." Subsequent to these comments, it set out the deficiencies included in Mr. Naperskow's February 28, 1991 memo.	Ex 1, Tab 78.
April 5, 1991	Letter from Jack M. Kay, Executive Vice President of Apotex to Dr. Somers	This letter follows up to the meeting Dr. Somers had with Mr. Kay "yesterday" and attached communications between HPB and Apotex between November 26, 1990 to March 8, 1991.	Ex 1, Tab 79.

April 6, 1991	Handwritten note from Mr. Rowsell to Dr. Somers.	He carefully reviewed the non-compliance letter with Ms. Thomas and Mr. Archibald and concluded "Apotex did not Use a Canadian reference standard nor did they Use the test product that would eventually be manufactured in Canada. We cannot accept secondary standards when we are dealing with people's health [short-hand revised]."	Ex 1, Tab 80.
April 25, 1991	Confidential letter from Dr. Sherman to Dr. Somers in response to the March 8, 1991, notice of non-compliance.	Similar to the letters above Dr. Sherman discussed his perception of the events and noted that Mr. Rowsell stated in the settlement discussions that the IR spectra comparisons and dissolution data "was the type of further data needed." He referred to (1) Apo-Timop, (2) Doxycin Capsules and Tablets and (3) Apo-Erythro-E-C as examples where "there is no policy requiring the reference be purchased in Canada." He concluded: "**Apotex is now suffering substantial damages from the delay in review and approval of Apo-Trazadone** [emphasis added]. We ask that you reconsider your position and confirm that our bioavailability study Using the reference purchased in the U.S. will suffice. If we do not receive such confirmation within a matter of days, we will have no alternative but to initiate another action in the Federal Court founded, inter alia, on **bad faith and on refusal to comply with the settlement agreement. We will also claim damages flowing from the delay in review and approval** [emphasis added]. Please reply promptly, as time is of the essence."	Ex 1, Tab 83.
May 1, 1991	Transcript of a telephone conversation between Dr. Sherman and Mr. Rowsell.	Dr. Sherman expressed a desire to resolve the matter without going to court: "But I mean if we have to go to court we will; it's a very important issue to us. Because so many products are at stake, and one of them is now AZT, Zidovudine." Amongst other things they disagreed over whether the data Dr. Sherman provided in the November 5, 1990 meeting was sufficient data. Mr. Rowsell stated they were prepared to look at any additional evidence, such as other analytical tests. When Dr. Sherman asked what type of evidence he should submit, Mr. Rowsell stated he could not do that	Ex 1, Tab 124.

		"Because, otherwise I'm doing your submission for you…It's not my job. My job is to evaluate the evidence that you submit."	
May 7, 1991	Letter from Dr. Somers to Dr. Sherman responding to the April 25, 1991 letter.	HPB acted and continues to act in good faith in review of the NDS for Apo-Trazadone and has and continues to comply with all agreements relating to said NDS. He then addressed the examples Dr. Sherman referred to in his letter finding each distinguishable from Apo-Trazadone and concluded "The Apo-Timop case must be regarded as an exception rather than the norm. You are well aware that the Directorate requires the Use of a Canadian reference product…the Drugs Directorate remains prepared to consider further evidence in relation to" said NDS.	Ex 1, Tab 85.
May 8, 1991	Fax from Dr. Sherman to Dr. Somers responding to the May 7, 1991 letter.	"Logically, the preferred reference is from the major market, as this is the reference to which the literature most closely relates…Please reconsider promptly as we are suffering damages."	Ex 1, Tab 86.
May 10, 1991	Letter from Dr. Sherman to Mr. Rowsell.	This related to the commencement of a review of the chemistry and manufacturing portions of Apotex's NDS for Apo-Zidovudine but Dr. Sherman stated "As you are well aware from the matter of Apo-Trazadone, it is our position that there is no logical or legal basis for your insistence on the reference being purchased in Canada." Then in relation to Apo-Zidovudine he stated "Please understand that in view of the economic importance and our firm belief that your insistence on the reference being purchased in Canada would be unreasonable and unlawful, we are determined to persevere in having this matter favourably resolved." He then threatened applying to the Federal Court for an order and stated "**We will also <u>mitigate damages</u> by commencing a repeat study and will hold HPB liable, for both the cost of the study and damages from delay in review and approval** [emphasis added]."	Ex 1, Tab 87.
May 13, 1991	Letter from Dr. Somers to Dr. Sherman responding to the	This is similar to other letters from Dr. Somers to Dr. Sherman, where the former reiterated that HPB communicated the requirement to Use a Canadian reference standard to Apotex as early	Ex 1, Tab 90.

	May 8, 1991 fax.	as December 11, 1981: "As with all procedures, the Drugs Directorate remains flexible and open to appropriate modification and adaptation. However, the general thrust of our policy… is considered to be fair, scientifically credible and consistent with good international practice."	
May 15, 1991	Memo from Dr. Cheryian to Dr. Nitchuk.	This is a re-papering of the above-referenced December 12, 1990 memo. Unlike the latter memo, this memo states "The DD policy requires that bioavailability comparisons be done with the generic product and the innovators product marketed in Canada. The manufacturer is trying to get around this requirement by attempting to establish that the U.S. and Canadian Desyrel formulations are identical." Moreover, the manufacturer data provided cannot alone "establish that the manufacturing processes of the Canadian and U.S. formulations are identical." He recommended providing a comment to Apotex stating "the data provided are not sufficient to establish that the Canadian and U.S.A formulations of Desyrel tablets are identical."	Ex 1, Tab 91.
May 15, 1991	Letter from Mr. Rowsell to Dr. Spino, now at Apotex, in response to the Apo-Trazad NDS and the additional information provided on November 5, 1990.	He repeated almost verbatim the language of the May 15, 1991 memo for example: "Although the FTIR spectra of the two formulations are almost identical, the conclusion that the two formulations are qualitatively and quantitatively identical is not scientifically tenable."	Ex 1, Tab 92.
May 29, 1991	Letter from Dr. Spino to Dr. Nitchuk following up to their meeting "a few weeks ago" with Mr. Rowsell, attachments included, he cc'd Dr. Sherman and	As offered in the meeting, Apotex enclosed additional information to "further support our contention that the U.S. and Canadian brands of Trazodone are indistinguishable." He enclosed the CHN analysis with raw data done by Guelph Chemical Laboratories and evaluated by Apotex's Director of Research and Development, Dr. Richard McKeag. They also noted that they would be providing a report from Jeff Hall an Applications scientist of	Ex 1, Tab 94.

	Dr. McKeag.	Perstorp Analytical who stated "the spectra of the U.S. and Canadian brands are indistinguishable." Dr. Spino concluded "I trust that you will find these data sufficient to demonstrate the similarity of the U.S. and Canadian brands. Any small difference which may exist is no more than that which would be expected"	
May 29, 1991	Letter from Dr. McKeag to Dr. Spino.	After analyzing Trazodone Hydrochloride samples for organic chemical components he concluded that "the U.S.A and Canadian Trazodone formulations are indistinguishable."	Ex 1, Tab 94.
May 31, 1991	Letter from Dr. Spino to Dr. Nitchuk, cc'ing Dr. McKeag and Dr. Sherman with enclosures following up to the May 29, 1991 letter.	He enclosed "a report from NIR Systems for their analysis of the U.S. and Canadian formulations of Trazodone. It is clear that the U.S. and Canadian brands are indistinguishable." He noted this is the final piece of information Apotex promised to HPB following the latter's request for "additional information on our claim that the U.S. and Canadian brands are indistinguishable."	Ex 1, Tab 95.
June 7 and 11, 1991	Letters from Elizabeth Wolfenden, Submission and Notification Administration Division of HPB to Dr. Spino.	In the June 7, 1991 letter Ms. Wolfenden confirmed receiving the May 29, 1991 letter and in the June 11, 1991 letter, she confirmed receiving the May 31, 1991 letter.	Ex 1, Tabs 96 and 97.
June 12, 1991	HPB, DBE Tracking System Submission.	Matter regarding the above letters assigned to Dr. Cheryian, with a handwritten note at the bottom stating he will "provide for additional information that Canadian and U.S. brand products are equivalent i.e. data in support of [shorthand revised]."	Ex 1, Tab 98.
June 21, 1991	Letter from Mr. Rowsell to Dr. Spino in response to the May 29 and 31, 1991 letters.	HPB concluded that based on the information provided Apotex did not establish "the equivalence of the reference standard Used by Apotex and the Canadian reference product." HPB remains prepared to consider further information to establish equivalency and continues to honour the settlement agreement but HPB suggested "that the most expeditious method to complete the Apo-Trazad New Drug Submission and consequently its review, would be the submission of a comparative	Ex 1, Tab 100.

		bioavailability study Using the Canadian reference product."	
June 27, 1991	Letter to Mr. Rowsell from Dr. Spino, cc'ing Dr. Sherman, responding to the June 21, 1991 letter.	Regarding Apo-Trazad he stated "I do not believe the correct decision was made in this instance because we have provided considerable evidence demonstrating that the product sold in the U.S. and in Canada are indistinguishable." He then focused on the pending decision regarding Apotex's pending study of "Apo-Zidovudine vs. Retrovir" and stated "Since we have shown that the formulation and release characteristics" in relation to Apo-Zidovudine "are indistinguishable, I trust that we can arrive at a reasonable conclusion" that the U.S. and Canadian versions of "Retrovir are the same…Otherwise it would appear to us that you have repudiated the agreement."	Ex 1, Tab 101.
July 2, 1991	Letter from Dr. Sherman to Dr. Somers following up to Dr. Spino's letter of June 27, 1991.	He then provided a long summary of the relevant issues for Apo-Trazadone and Apo-Zidovudine, elaborating on some of the considerations from the June 29, 1989 letter and stated the refusal to accept the NDS's for those drugs on "the purported basis that the reference must be purchased in Canada is discriminatory." He listed examples of HPB accepting generic products in Canada on the basis of purchasing the reference outside Canada: (1) theophylline tablets, (2) amoxicillin tablets, (3) tamoxifen tablets, (4) timolol maleate ophthalmic, (5) doxycycline tablets and capsules, and (6) erythromycin P-C tablets and E-C capsules. He then stated Apotex complied with the settlement agreement by providing for both Trazodone and Zidovudine "extensive comparisons which confirm the U.S. and Canadian references indistinguishable." However, "MR. Rowsell has reverted to the position that laboratory comparisons will not suffice and that approval can be obtained <u>only</u> on the basis of certification by the originator or a bioavailability study against the reference purchased in Canada [emphasis in original]." He urged HPB to abandon its position or "comply in good faith with the Settlement Agreement." If HPB failed to do so "we will have no alternative but to promptly proceed with further steps in the	Ex 1, Tab 102.

		Federal Court. **In view of the severe damages now accruing, we will not limit our action to an Application for an Order in the nature of mandamus, <u>but we will also pursue a statement of claim for damages</u>** [emphasis added]."	
July 5, 1991	Memo from Dr. Cheryian to Dr. Nitchuk.	This is a discussion of the CHN analysis for the batches of Canadian and U.S. formulations and a finding that "The above evidence does not contribute much to support the equivalency of the Canadian and U.S. formulations…the data does not unequivocally establish the chemical similarity of the two formulations." He reiterated many of the issues from his May 15, 1991 review and noted issues relating to the physical nature of the components potentially arising from "the actual manufacturing process have not been satisfactorily dealt with."	Ex 1, Tab 103.
July 10, 1991	Letter from Mr. Rowsell to Dr. Spino in response to the letter of June 27, 1991.	He emphasized that HPB "consistently stated that a comparative bioavailability study should be performed utilizing the currently marketed Canadian drug formulation as the essential reference standard."	Ex 1, Tab 104.
July 10, 1991	Affirmed Affidavit of Dr. Sherman for Judicial Review II.	Regarding the provision in the settlement agreement on "evidence to establish the equivalence between the Canadian and non-Canadian reference standards", Dr. Sherman stated "What was contemplated and specifically acknowledged by Mr. Rowsell was laboratory comparisons of Canadian and U.S. references to confirm the absence of any significant differences in their chemical composition and dissolution characteristics. We had already performed such comparisons between Canadian and U.S. samples of the reference brand for Apo-Trazad, and in the course of the discussions I handed the data to Mr. Rowsell. Mr. Rowsell responded that this was 'exactly the sort of additional data I am talking about.'"	Ex 3, Tab 2.
July 17, 1991	Letter from Dr. Somers to Dr. Sherman in reply to the July 2, 1991 letter.	"The Drugs Directorate maintains that it is good policy to require that the reference product be purchased from the Canadian market." After asserting that the Drugs Directorate adhered to the Settlement Agreement he concluded that "the Drugs Directorate has examined additional evidence provided by Apotex Inc. and	Ex 1, Tab 105.

		determined that the data were not sufficient to establish equivalency. Although the data is persuasive with respect to chemical equivalency, it does not address the performance characteristics of the product."	
July 17, 1991	**Judicial Review II:** Apotex filed a **Notice of Motion for judicial review** on behalf of Apotex with the Federal Court of Canada Trial Division (T-1877-91).	Apotex requested an order directing the Minister to review Apotex's NDS for Apo-Trazad and Apo-Zidovudine with identical relief requested as in the first judicial review proceeding for this matter.	Ex 3, Tab 1.
July 31, 1991	Letter from Dr. Sherman to Dr. Somers, responding to the July 17, 1991 letter.	"How could there have been a settlement agreement if your position is no different after the agreement than before? I believe that each and every one of the 'comments' made by you is untenable. Moreover, taken together they appear to demonstrate an intransigent refusal to act in good faith. Damages to Apotex are rapidly accruing, and I urge you again to immediately confirm the acceptability as our submissions, so as to avoid the need for us to pursue the Notice of Motion and a claim for damages."	Ex 1, Tab 111
September 10, 1991	Sworn affidavit of Mr. Rowsell for the purpose of Judicial Review II.	"[W]e agreed in the settlement agreement to consider any evidence which Apotex might see fit to submit to satisfy us that the U.S. reference standard Used by Apotex in this case was equivalent to the product marketed in Canada…in good faith, we reviewed all of the materials submitted to the Department by Apotex…The director was not persuaded that the reference standard Used by Apotex was equivalent to a product marketed for sale in Canada, and was not persuaded that the evidence submitted respecting Apo-Trazad was sufficient to establish that the product was safe and effective as required by regulation C.08.002."	Ex 3, Tab 4.
September 20, 1991	Letter via courier to the Director of the Bureau of Pharmaceutical	In response to the non-compliance letter of March 8, 1991, Apotex submitted substantial additional data to demonstrate that the U.S. and Canadian brands of Desyrel "are	Ex 1, Tab 115.

	Surveillance of HPB from Mr. Hems, with enclosures.	indistinguishable" and also to demonstrate the "similarity" of said brands: "Therefore, the comparative bioavailability study done with the U.S. brand should be acceptable to HPB."	
September 26, 1991	Letter from Ms. Wolfenden to Mr. Hems.	Confirming receipt of the letter and additional information from September 20, 1991.	Ex 1, Tab 117.
October 1, 1991	Affirmed supplemental affidavit of Dr. Sherman in response to Mr. Rowsell's September 10, 1991 affidavit for the purpose of Judicial Review II.	Dr. Sherman stated the wording of the initial draft settlement agreement proposed in the above-referenced November 13, 1990 letter "could have been taken to mean that Apotex would be required to establish both clinical and therapeutic equivalence of the Canadian and foreign references, whereas the essence of the settlement discussions was that Apotex would submit as further evidence only laboratory comparisons of two references and that H.P.B. would accept the two references were equivalent if laboratory comparisons disclosed no difference." As a result HPB changed the wording of the settlement agreement, "It was intended that: (a) chemical equivalence of Apotex's product would be established by the chemistry and manufacturing section of Apotex's submission (as is always the case); (b) therapeutic equivalence of Apotex's product would be established by a bioavailability study (which demonstrated therapeutic equivalence of Apotex's product to the U.S. reference), together with the laboratory comparisons of the two references to confirm that the two references were chemically (and thus therapeutically) equivalent to each other."	Ex 3, Tab 5.
November 29, 1991	Letter from Dr. Somers to Mr. Hems in response to the September 20, 1991 letter.	He advised that the submission status for Apo-Trazad "is in active" while HPB awaits further information in response to the Notice of Non-Compliance of March 8, 1991 because "this New Drug Submission does not comply with the requirements of Section C.08.002 of the Regulations in that it has failed to establish the safety and efficacy of Apo-Trazad Tablets in comparison to a Canadian reference standard."	Ex 1, Tab 121.

		HPB remained prepared to review further information from Apotex "in order to establish the equivalence of the reference standard Used and the Canadian reference standard."	
December 4, 1991	Without prejudice letter from Ms. Thomas from Mr. Radomski via telecopy.	Mr. Radomski re-emphasizes Apotex's belief in the appropriateness of Using a foreign reference brand and stated "the Apotex bioavailability studies are appropriate."	Ex 1, Tab 122.
1992	Health Products and Food Branch Guidance Document: *Guidance for Industry: Conduct and Analysis of Bioavailability and Bioequivalence Studies – Part A: Oral Dosage Formulations Used for Systemic Effects*. Published by the Authority of the Minister of Health.	Regarding the selection of a reference product: "For a new drug substance (i.e., the first market entry), an oral solution should be Used as the reference product when possible…In bioequivalence studies, the reference product is: • a drug product that has been issued a notice of compliance pursuant to section C.08.004 of the *Food and Drug Regulations*, and is currently marketed in Canada by the innovator, or • A drug product acceptable to the Director.	Exhibit 10.
April 15, 1992	Memo from Mr. Ward to Dr. Nitchuk on the dissolution issues regarding the data from Mr. Hems of September 20, 1991, attachment included.	He set out to determine if Apotex demonstrated the U.S. and Canadian marketed Desyrel tablets as "equivalent" or "indistinguishable" by physico-chemical comparison including dissolution testing. He concluded "It is generally accepted that comparative dissolution profile analyses cannot replace bioavailability studies as a means of establishing 'bioequivalence' between two different products unless an in-vitro/in-vivo correlation has been demonstrated [emphasis in original]." He provided an attachment in the original submission for Apo-Gemfibrozi to demonstrate the "danger in Using dissolution data as an indicator of product equivalency."	Ex 1, Tab 126.
April 15, 1992	Memo from Mr. Ward to Dr. Nitchuk regarding the September 20,	First he notes Apotex advised of their intention to change the brand name of the product from Apo-Trazad to Apo-Trazadone. In discussing the dissolution data, the memo addressed	Ex 1, Tab 127.

	1991 data, specifications attached.	comments 2, 10 and 11(a) in HPB's March 8, 1991 letter of deficiencies to Apotex.	
April 16, 1992	Facsimile to Mr. Radomski from Ms. Thomas, cc'ing Mr. Archibald.	This confirms telephone conversations between Mr. Radomski and Ms. Thomas on April 10, 14, and 15, 1992 regarding the review of dissolution studies which Apotex submitted for Apo-Trazad: "I am advised that all that was submitted by Apotex with respect to the critical equivalence comparison between the two originators of Trazad…was a statement that the dissolution profiles were similar. There was no back-up raw data." She reaffirmed HPB will be happy to review raw data on the comparison of the two originators to prove therapeutic equivalence.	Ex 1, Tab 128.
April 20, 1992	Facsimile from Ms. Thomas to Mr. Radomski, cc'ing Mr. Archibald.	"With respect to dissolution studies submitted to establish therapeutic equivalence of the U.S. and Canadian originator's of Trazad, as you know, it is the Respondent Minister's position that the dissolution methodology may not be discriminatory enough to detect changes…this issue is on the edge of the known learning in this area and an adequate dissolution methodology can only be designed post facto."	Ex 1, Tab 129.
April 21, 1992	Comparative Dissolution rates of Desyrel Tablets U.S. vs. Canadian, signed by Mr. Hems.	This report sets out the dissolution rates of U.S. and Canadian Desyrel 100 mg tablets and concludes that "The dissolution profile of the Canadian marketed Desyrel is indistinguishable from that of the U.S. marketed Desyrel." Dr. Sherman admitted in cross-examination that it appears dissolution occurred within 15 minutes **93%** of the time.	Ex 1, Tab 130.
April 27, 1992	Letter via courier from Mr. Hems to Dr. Nitchuk, attaching the April 21, 1992 report.	Apotex enclosed full details for the comparative dissolution rates of two lots of Canadian and two lots of U.S. Desyrel tablets 100 mg. He noted "All lots of both strengths of Desyrel exhibit approximately **95%** dissolution within 15 minutes, regardless of whether purchased in the U.S. or Canada. Clearly, U.S. and Canadian Desyrel are not distinguishable from each other on the basis of dissolution…We believe that this information, together with the chemical comparisons…make it clear beyond any reasonable doubt that Canadian Desyrel is the same product as U.S. Desyrel [emphasis	Ex 1, Tab 130.

		added]."	
April 28, 1992	Note with two sets of handwriting, one belonging to Dr. Nitchuk the other to Mr. Ward.	Dr. Nitchuk provided the April 27, 1992 dissolution data to Mr. Ward and instructed Mr. Ward to prepare comments "concerning all dissolution data submitted to establish U.S. and Canadian Desyrel therapeutically equivalent." It appears to tell Mr. Ward to find no therapeutic equivalence since Apotex must establish "a relationship between the <u>in vitro</u> (dissolution data) and <u>in vivo</u> (bio study) methods [emphasis in original]" notwithstanding that "the submitted data" discloses no difference. Mr. Ward then stated he looked at the report and agreed with the conclusion of Mr. Hems in the April 27, 1992 letter.	Ex 1, Tab 131.
October 9, 1992	**Six years before Apotex filed its Statement of Claim for the present action (T-1930-98).**		
Unknown date in 1993	Admitted Facts: Notice of Compliance issued to Pharmascience.	Pharmascience received a Notice of Compliance for its brand of Trazad tablets sold under the name PMS-Trazad. Pharmascience was the first entrant in the generic market for Trazad tablets.	Ex 5.
January 19, 1993	*Apotex Inc v Canada (Attorney General) et al* (1993), 59 FTR 85.	MacKay J dismissed Apotex's application for judicial review for Apo-Zidovudine as moot and for Apo-Trazadone on the ground that: the fact that in many previous submissions by Apotex itself bioavailability studies were included with reference to a Canadian standard product, and HPB's reference to practices followed in some other countries, lead me to conclude that there is no basis for this Court to conclude to determine that the HPB requirement is patently unreasonable or beyond the discretion of the Director under section C.08.002 of the regulations (Paragraph 86).	Ex 3, Tab 19.
February 2, 1993	Letter from Dr. Sherman to Dann N. Michols,	He requested Mr. Michols direct the Bureau of Drug Surveillance to complete a review of its NDS for Apo-Trazadone and disclose any	Ex 1, Tab 139.

	Assistant Deputy Minister, National Pharmaceutical Strategy at HPB.	deficiencies in order to comply with the Settlement Agreement of November 1990. He cited MacKay J criticisms of HPB's conduct to emphasize his allegation of unfair treatment from HPB.	
February 8, 1993	Apotex's Notice of Appeal (A-135-93).	Apotex filed an appeal of MacKay J's decision to the Federal Court of Appeal.	Ex 3, Tab 20.
October 7, 1993	Handwritten note from Richard Pike of HPB.	Mr. Pike reviewed the Apo-Trazad dissolution data of April 27, 1992 on or around April 28, 1992 and "found to be similar and we concluded that the two products have similar dissolution rates. No deficiencies were identified and consequently no further questions were put to Apotex."	Ex 1, Tab 142.
October 14, 1993	Fax from Mr. Michols, Executive Director of the National Pharmaceutical Strategy at the Drugs Directorate, to Ms. Carman, cc'ing Mr. Archibald.	Mr. Michols advised that he met with Dr. Sherman on October 7, 1993 regarding the NDS for Apo-Trazadone. He undertook to write to Dr. Sherman in the immediate future on the results of HPB's analysis of the dissolution data setting out any problems or deficiencies and HPB's decision on where the NDS stands. He added: "we owe Apotex a full explanation of what the deficiencies in its submissions are", and if said deficiencies are scientific then state "how the deficiency analysis could be improved...I have the feeling that our practices and maybe even our policies have been inconsistent in the past. We have new management across the board. I would like clear signals on what our policies and practices will be. If I have not made myself clear on this matter, please call me and we can discuss."	Ex 8.
January 4, 1994	Without prejudice letter delivered by telecopy and by hand from Mr. Radomski to Ms. Thomas.	Apotex obtained and reviewed Mr. Ward's memorandum of April 15, 1992 through Access to Information and stated "your client has failed to review the dissolution data submitted in conjunction with and in light of the finding of chemical equivalence of the U.S. and Canadian reference brands…it follows that your client has failed not only to abide by the terms of the settlement agreement but to discharge its statutory obligation…Apotex has never taken the position that comparative dissolution data for <u>different</u> products would be sufficient in the absence of a comparative bioavailability	Ex 1, Tab 144.

		[emphasis in original]."	
January 8, 1994	Letter from Dr. Sherman to Mr. Michols, following up to the October 7, 1993 meeting.	Dr. Sherman did not receive a response and noted the Court scheduled the appeal for this matter for February 8, 1994: "Apotex has already suffered great harm from a refusal which was, we believe, both arbitrary and contrary to an explicit agreement…We urge you to bring this matter to an end by now considering our data in light of the relevant and agreed principles and issuing a notice of compliance."	Ex 1, Tab 147.
January 14, 1994	Fax from Ms. Carman to Mr. Michols, with attachments.	Ms. Carman forwarded "Letter from Dr. Sherman as requested." This contained two letters from Dr. Sherman, one from February 2, 1993, the other from January 8, 1994, both referenced above.	Ex 1, Tab 147.
January 14, 1994	Facsimile from Ms. Carman to Mr. Archibald and Mr. Michols with attachments.	Ms. Carman stated "The attached letter should address our outstanding commitment to Apotex." She attached two versions of the same letter for Mr. Michols to send to Dr. Sherman. Both would respond to Dr. Sherman's letter of January 6, 1994 and the meeting of October 7, 1993. Both versions contained the following statement in response to the review of the April 15, 1992 dissolution data: "As no deficiencies were identified with this dissolution data, when Used as a routine quality control tool, a request for further information was not required and Apotex Inc. was not contacted. It remains our position that comparative dissolution profiles cannot replace comparative bioavailability studies as a means of establishing bioequivalence between two products unless an in-vivo/in-vitro correlation has been demonstrated. No such data has been provided with respect to this submission [emphasis in original]."	Ex 1, Tab 148.
January, 1994	An "URGENT DRAFT" of the January 14, 1994 draft letter.	Ms. Carman marked this draft as urgent, and the draft included several handwritten insertions, and some deletions.	Ex 1, Tab 149.
January, 1994	This is a version of Mr. Radomski's letter of February 9, 1994.	The letter contains several handwritten notations in the margin by Ms. Carman where she stated in testimony that she wrote these to set out the parameters for resolution which they discussed. These notations indicated that (1) Apotex did	Ex 1, Tab 150.

		not establish chemical equivalence (2) dissolution studies may be capable of demonstrating bioequivalence without the necessity of a comparative bioavailability study, however, Ms. Carman stated in her testimony that HPB did not consider dissolution standards an acceptable standard on their own to establish bioequivalence between two products, and (3) HPB would require in vivo/vitro correlation.	
February 17, 1994	Memorandum from Dr. Nitchuk to Ms. Carman.	As a result of communications with Mr. Radomski, the parties agreed to adjourn the appeal to April 25, 1994 in order to re-review the reference product. The re-review would take into account material Apotex provided on November 5, 1990, May 29, 1991, May 31, 1991 and September 20, 1991.	Ex 1, Tab 152.
February 26, 1994	Letter to Mr. Radomski from John Vaissi Nagy from Department of Justice.	HPB "acknowledges the chemical equivalence of the Canadian and U.S. reference brands, as set out in the reasons for Order of MacKay J." He stated HPB would review the data which Dr. Nitchuk discussed in his February 17, 1994 memo. He also noted "it is hypothetically possible that appropriately designed dissolution studies could be capable of demonstrating bioequivalence without the necessity of a comparative bioavailability study", however "The scientific conclusion as to whether in vitro dissolution can ever be Used as a measure of in vivo bioequivalence awaits further study [emphasis in original]." Finally he advised Mr. Radomski that HPB intends to implement this agreement as expeditiously as possible upon its finalization.	Ex 1, Tab 153.
April 8, 1994	Memo from Mr. Ward to the Director, including Ms. Carman's signature, with attachments.	After reviewing the above-referenced dissolution data discussed in the February 17, 1994 memorandum, he maintained "that Apotex has not adequately established the bioequivalence of the Canadian and U.S. Desyrel drug products." He noted that Apotex did not demonstrate from the data submitted that "any of the dissolution conditions examined are capable" of "detecting differences in manufacturing, etc., which could impact on in vivo behaviour [emphasis in original]." Some attachments included the November 2, 1990 data, and his memo to Dr. Nitchuk of April1 15,	Ex 1, Tab 159.

		1992.	
April 8, 1994	Letter from Ms. Carman to Dr. Sherman, attaching Mr. Ward's April 8, 1994 report.	Ms. Carman advised Apotex that HPB would not issue a Notice of Compliance as a result of the re-review of the data Apotex submitted "for the purpose of establishing the therapeutic equivalence of the Canadian and U.S. reference products."	Ex 1, Tab 159.
May 16, 1994	Minutes of a meeting between Ms. Carman, Mr. Ward, Dr. Spino and Mr. Hems. The meeting occurred for HPB to answer Apotex's questions regarding Mr. Ward's report of April 8, 1994.	Ms. Carman and Mr. Ward stated that "the Directorate was not intransigent and would seriously consider further data." Ms. Carman "also emphasized that this case was a watershed for many issues; policy definitions are appropriately made subsequent to a scientific process rather than as a consequence of litigation." However, Mr. Ward noted that Apotex did not prove (1) the U.S. and Canadian reference brands "were in fact 'the same' as the company had no knowledge of the innovator's manufacturing process and hence whether or not production differences existed and (2) the QC dissolution test conditions examined are capable of detecting differences in manufacture of the Desyrel products which could impact on <u>in vivo</u> performance [emphasis in original]."	Ex 1, Tab 160.
May 16, 1994	Overhead material Dr. Spiro provided to Mr. Ward by hand at the May 16, 1994 meeting.	The material concluded that the evidence Apotex submitted "is sufficient to conclude that the U.S. and Canadian reference products are the same, or not sufficiently different to warrant an additional direct comparison of the bioavailability of the Apotex product with the Canadian reference product, assuming that it is bioequivalent with the U.S. product.	Ex 1, Tab 160.
May 31, 1994	Letter to Ms. Carman from Mr. Hems cc'ing Dr. Sherman and Dr. Spino as a follow up to the May 16, 1994 meeting.	"Notwithstanding the apparent lack of necessity of anything further, we agreed at the meeting of May 16th, 1994, that we would conduct a series of dissolutions studies to further demonstrate that our method is discriminating and that there is no significant difference in the dissolution profiles between the U.S. and Canadian Desyrel products." Mr. Hems attached the additional data and concluded the dissolution methodology enables Apotex to distinguish between two bioequivalent products: "It also demonstrates that there are no significant differences between the mean profiles of the U.S. and Canadian Desreyl products."	Ex 1, Tab 162.

June 2, 1994	Action request from Ms. Carman to Mr. Ward.	Ms. Carman requested that Mr. Ward contact her without delay regarding the Apo-Trazadone NDS.	Ex 1, Tab 163.
June 23, 1994	Unsigned report from Mr. Ward to Ms. Carman, regarding the May 31, 1994 comparative dissolution data.	After reviewing the data, he concluded "I have no outstanding concerns regarding the potential inequivalence of U.S. and Canadian marketed Desyrel…Apotex has provided sufficient evidence to allay any reasonable concerns that said products could in general perform differently in vivo [emphasis in original]."	Ex 1, Tab 164.
June 23, 1994	Email from Genette Gratton, Ms. Carman's assistant to Mr. Ward.	She reminds Mr. Ward of his June 24, 1994 deadline to provide his reply in relation to the dissolution testing and asks if he needs an extension.	Ex 1, Tab 165.
June 28, 1994	Email from Ms. Gratton to Mr. Ward.	Ms. Gratton reminds him of the next day deadline for the above-referenced reply and asks if he needs an extension.	Ex 1, Tab 166.
June 28, 1994	Email from Mr. Ward to Ms. Gratton.	He stated the "Draft is complete. Should I simply transfer the file via WP Office for Mary's comment?"	Ex 1, Tab 166.
July 7, 1994	Email from Mr. Ward to Ms. Carman, cc'ing Norm Pound.	"Would you like to discuss my draft report before I go on vacation (next week)?"	Ex 1. Tab 167.
July 29, 1994	Email from Ms. Carman to Mr. Ward and Mr. Pike, cc'ing Mr. Pound.	In the process of developing a draft report: "I would appreciate a collaborative effort between the two of you to establish a listing of data requirements that we would want in order to establish chemical equivalence between the two products…I know we are all pressed right now but this problem will require resolution in the early fall and we need something to work with. As I will be on leave beginning August 13, there is no sense in asking for this sooner."	Ex 1, Tab 168.
August 5, 1994	Fax from Dr. Spino to Ms. Carman, cc'ing Dr. Sherman.	"We are waiting for HPB to inform us that they are willing to accept the evidence submitted, demonstrating that the U.S. and Canadian reference brands of Trazodone are indistinguishable."	Ex 1, Tab 169.
August 15, 1994	Facsimile from Ms. Carman to Dr. Spino responding to August 5, 1994 fax.	"Received your fax – due to impending holiday schedules this file is planned to be addressed in early September."	Ex 1, Tab 170.
September	Email from Ms.	"I have spoken to peter about the increased	Ex 1,

9, 1994	Carman to Mr. Pound.	urgency of this file. Legal will try to buy us 2-3 weeks to finalize our position…this one has to move fast or we will be stuck with our previous acceptance criteria."	Tab 171.
October 18, 1994	Mr. Hem's Record of Telephone Communication to Ms. Carman.	Ms. Carman returned Mr. Hems's call regarding the status of Apo-Trazadone and left a voicemail: "It is currently under discussion with legal council so I'm not sure I can tell you any more."	Ex 1, Tab 172.
November 14, 1994	Email from Ms. Carman to Linda Muldoo, Mr. Jeffs's assistant.	She advised that in spite of Mr. Jeffs's concerns they "have a submission that from a pharmaceutical chemistry perspective is acceptable…It is now necessary for the Directorate to review the submitted bioavailability studies and to finalize this submission (Apo-Trazad). As soon as this safety and effectiveness review is complete there are several other submissions waiting which must be dealt with."	Ex 1, Tab 175.
December 1, 1994	Signed final report, dated December 1, 1994 from Mr. Ward to Ms. Carman for action.	The report provided "In light of the Crown's acknowledgement of chemical equivalence, the nature of the drug substance, and the results of comparative dissolution analyses in a variety of media over the physiological pH range, I conclude that no basis remains for articulating concerns regarding the potential inequivalence of U.S. and Canadian marketed Desyrel.	Ex 1, Tab 197.
December 7, 1994	Admitted Facts: Notice of Compliance issued to Novopharm.	Novopharm received a Notice of Compliance for its brand of Trazad tablets sold under the name Novo-Trazad. Novopharm was the second entrant in the generic market for Trazad tablets.	Ex 5.
December 16, 1994	Signed memorandum from Mr. Ward prepared for Ms. Carman.	Mr. Ward noted that his final report of December 1, 1994 was a "slightly amended copy" of his June 23, 1994 unsigned report. "I would be happy to discuss this report with you at your earliest convenience."	Ex 1, Tab 197.
December 19, 1994	Letter from Dr. Sherman to Ms. Carman.	Dr. Sherman noted that Ms. Carman stated to Dr. Spino "that review was to commence on December 15, 1994 and would be completed within 120 days." He wrote to ensure HPB understood the urgency of completing the review because "two weeks ago a Notice of Compliance for Trazodone hydrochloride tablets was issued to Novopharm, our principal competitor…it is now imperative that we come	Ex 1, Tab 182.

		to the market within a few days so as not to let Novopharm have a lead over Apotex."	
December 20, 1994	Email from Mr. Pound to J Ogilvi of HPB, cc'ing Mr. Jeffs, A. Napers, Ms. Carman and Dr. Nitchuk regarding the December 19, 1994 fax.	"We are not requesting overtime to address this issue at this time. The NOC can not be issued until the court case is 'finalized' (possibly in the next few days), but we do wish to proceed with the review as a TOP priority."	Ex 1, Tab 186.
December 21, 1994	Clarifax from Dr. Nitchuk to Mr. Hems.	Dr. Nitchuk requested "updated label drafts for the 50, 100 and 150 mg dosage forms, and if appropriate, a product monograph" in order for HPB to "continue our evaluation of the safety and efficacy portion" of the NDS for Apo-Trazadone.	Ex 1, Tab 187.
December 21, 1994	Email from Mr. Pound to Ms. Carman, J Ogilvi, cc'ing Mr. Jeffs, A. Napers, Mr. Ward and Dr. Nitchuk.	He noted that Mr. Ward informed him that Mr. Ward "is just now in the process of finalizing his review of the data submitted by Apotex." Mr. Pound asked whether "we are now satisfied with the data submitted and that the court case is 'finished'?" Moreover, "the issue concerning the equivalency of the Barr product Used in the bio-study and the Apotex product to be manufactured and sold in Canada has not been addressed."	Ex 1, Tab 188.
December 21, 1994	Email from Mr. Ward to Mr. Jeffs.	Mr. Ward advised that he spoke with Mr. Pound and mentioned "that I had finalized the Apo-Trazad reference standard report."	Ex 1, Tab 189.
December 22, 1994	Letter from Mr. Hems to Dr. Nitchuk in response to the December 21, 1994 facsimile.	Mr. Hems provided the requested additional information: "Updated label drafts and an updated Product Monograph as appended."	Ex 1, Tab 192.
December 23, 1994	Correspondence Control Manger routing slip from Mr. Ward sent to Ms. Carman for action.	Mr. Ward delivered his final report signed on December 1, 1994 with the memo of December 16, 1994 to Ms. Carman with the note that he would like to discuss it at Ms. Carman's earliest convenience.	Ex 1, Tab 197.
January 3, 1995	Email from Ms. Carman to Mr. Ward.	"I have read your report and do not see further difficulties presented … just the same old problems with how to extricate ourselves from this one. If you want to discuss, please drop by."	Ex 1, Tab 201.

January 6, 1995	Fax from Mr. Nagy to Mr. Radomski with an attached "Release".	HPB "is attempting to expedite the review. It may be possible to finish the Apo-Trazadone review in less than 120 days indicated in Ms. Carman's letter. Hence I would be grateful if you could have the accompanying release signed, sealed and witnessed and returned to me at your earliest convenience." This release would discharge the Crown "from any and all manner of claims, actions, causes of action, debts, demands, dues, covenants, bonds, contracts, and claims for interest and costs, which against the said Releasees we may ever have had, may have or hereinafter can, shall and may have for any reason of any cause…related to Apotex Inc.'s Trazodone."	Ex 1, Tab 203.
January 9, 1995	Letter from Mr. Radomski to Mr. Nagy rejecting the request for a Release.	Following up with an exchange of telephone messages: "I am at a loss to understand the basis upon which your client now demands a release in return for the grant of a Notice of Compliance for Apo-Trazadone."	Ex 1, Tab 204.
January 30, 1995	Letter from Ms. Thomas to Mr. Radomski, cc'ing Mr. Archibald in response to Mr. Radomski's January 9, 1995 letter.	HPB confirmed to her that "the re-review of this submission is proceeding expeditiously in accordance with H.P.B. procedures…Needless to say, I would not attempt to seek any agreements which would limit legal recourse which your client may properly have against mine. However, to use a phrase from your letter to John Vassi Nagy dated January 9, 1995 and mine to you, dated January 13, 1995, my client hopes to effect 'an end to the matter' once the re-review of the submission is complete."	Ex 1, Tab 210.
February 6, 1995	Letter from Dr. Sherman to Ms. Carman.	"You have still not answered to, or even acknowledged receipt of, my letter of December 19, 1994, or my letter January 16, 1995. We are now being caused to miss the submission deadlines for the July 1995 editions of various provincial formularies."	Ex 1, Tab 216.
February 8, 1995	Memo from Mr. Pound to Ms. Carman with a handwritten note from Ms. Carman at the bottom of the page.	Mr. Pound advised Ms. Carman that Dr. Nitchuk recommended they ask for "information again" because "it is our 'suspicion' that comparative data for the Canadian product exists." Ms. Carman wrote: "Norm- either we <u>are</u> or <u>not</u> satisfied. I do not support continued clarifax requests [emphasis in original]."	Ex 1, Tab 218.
February	Safety and	Dr. Nitchuk advised that Apotex	Ex 1,

14, 1995	Efficacy Report from Dr. Nitchuk to Mr. Pound.	"misunderstood our request" for clarification. He then recommended requesting Apotex "submit all bioavailability data comparing the Apo-Trazadone formulations with Desyrel purchased from the Canadian market." He concluded "the test product has not met our current requirements for second entry products in that the comparative bioavailability study was not performed Using 'the corresponding currently marketed Canadian drug formulation as the essential reference standard.'"	Tab 220.
February 16, 1995	Memo from Mr. Pound to Ms. Carman.	Notwithstanding Dr. Nitchuk's recommendations in the February 14, 1995 report: "I concur with you that another clarifax is not appropriate at this time, and in light of the result of the litigation between ourselves and the sponsor, a NOC should be issued. As requested, please find attached a NOC for this product."	Ex 1, Tab 221.
February 28, 1995	**Notice of Compliance to Apotex** with attention to Mr. Hems from Mr. Michols.	HPB issued a Notice of Compliance for the NDS for Apo-Trazadone D tablets.	Ex 1, Tab 224.
December 5, 1995	Letter from Mr. Nichols to various governments, and the pharmaceutical industry.	Policy Issue from the Drugs Directorate: *Canadian Reference Product*. It sets out the compliance criteria "In order for a drug product purchased in another country to be considered acceptable for Use as Canadian Reference Product."	Ex 1, Tab 227.
October 9, 1998	**Apotex filed its Statement of Claim for this action (T-1930-98).**		

FEDERAL COURT

SOLICITORS OF RECORD

DOCKET:	T-1930-98
STYLE OF CAUSE:	APOTEX INC. v HER MAJESTY THE QUEEN
PLACE OF HEARING:	TORONTO, ONTARIO
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APPEARANCES:

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