CANADA / JUDGMENT

AstraZeneca Canada Inc. v. Apotex Inc.

2017 FC 726

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Dockets: T-1409-04

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Citation: 2017 FC 726

Ottawa, Ontario, July 26, 2017

PRESENT: The Honourable Mr. Justice Barnes

Docket: T-1409-04

BETWEEN:

ASTRAZENECA CANADA INC. AND AKTIEBOLAGET HÄSSLE

Plaintiffs

(Defendants by Counterclaim)

and

APOTEX INC.

Defendant

(Plaintiff by Counterclaim)

Docket: T-1890-11

AND BETWEEN:

ASTRAZENECA AB AND AKTIEBOLAGET HÄSSLE

Plaintiffs

(Defendants by Counterclaim)

and

APOTEX INC.

Defendant

(Plaintiff by Counterclaim)

Docket: T-2300-05

AND BETWEEN:

APOTEX INC.

Plaintiff

and

ASTRAZENECA CANADA INC.

Defendant

PUBLIC JUDGMENT AND REASONS

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[1] In these bifurcated proceedings, AstraZeneca Canada Inc., Aktiebolaget Hässle and AstraZeneca AB [collectively AstraZeneca] seek an accounting of the profits earned by Apotex Inc. [Apotex] from the infringement of AstraZeneca's Canadian Letters Patent No 1,292,693 [693 Patent]. In the liability phase of the infringement actions (Court dockets T-1409-04 and T-1890-11), the Court found in favour of AstraZeneca: see AstraZeneca v Apotex, 2015 FC 322, 134 CPR (4th) 1, aff'd in part 2017 FCA 9, [2017] FCJ No 22 (QL). The commercial product covered by the 693 Patent is an omeprazole formulation marketed by AstraZeneca in Canada under the trade name LOSEC. The period of infringement by Apotex runs from September 5, 2003 to December 3, 2008.

[2] In Court docket T-2300-05 Apotex, in turn, seeks an offset for its section 8 damages for being held out of the Canadian market for its generic omeprazole formulation [Apo-Omeprazole] between January 3, 2002 and December 30, 2003 by reason of AstraZeneca's failed Patented Medicines (Notice of Compliance) [NOC] application concerning its 762 Patent.

[3] All of these references were consolidated by a case management Order dated December 11, 2013 and were tried together at Toronto.

[4] To their considerable credit, the parties have resolved most of their quantification issues and have reduced their agreement to writing [see Exhibit AZ 24]. They have also agreed that their respective accounting experts will adjust their calculations as required by the streamlining agreement and by any other issues resulting from the Court's Judgment. Any remaining points of disagreement between the accounting experts will be referred to the Court for final resolution.

[5] The parties have left with the Court the following matters for determination:

(a) During the period of infringement of the 693 Patent, did Apotex have an available non-infringing alternative [NIA];

(b) How should the Court reconcile the section 8 Judgment in favour of Apotex in Court docket T-2300-05 with the infringement Judgment in favour of AstraZeneca in Court dockets T-1409-04 and T-1890-11;

(c) With respect to Apotex's profits from the infringement of the 693 Patent, what allowance should be made for profits-on-profits; and

(d) With respect to the infringement of the 693 Patent, what allowance is required having regard to the United States District Court award for the infringement of the United States Patent No 4,786,505 [505 Patent] and Apotex's satisfaction of that award.

[6] The matter of costs is to be left pending further submissions from the parties.

I. During the Period of Infringement of the 693 Patent, Did Apotex Have an Available Non-Infringing Alternative [7] It is now well established in Canadian law that a NIA defence is available to a patent infringer to potentially reduce an innovator's claim to damages or to the recovery of the infringer's profits.

[8] The onus rests on Apotex to prove that a NIA was available and at what cost. This point was made in Reading & Bates Construction Co v Baker Energy Resources Corp (1992), 44 CPR (3d) 93 at pp 106-107, 56 FTR 22 (FCTD), aff'd (1994) 58 CPR (3d) 359, 175 NR 225 (FCA), where Justice Barry Strayer held:

I also agree with the learned referee's conclusions of law that the onus is on the defendant to prove that an alternative non-infringing method existed and the costs of using that method. Although the defendant cited several cases to the contrary, these were cases from the Circuit Courts of the United States, one of which was over 100 years old and none of which were less than about 50 years old. On the other hand, I believe that such Canadian jurisprudence as exists is consistent with the burden being on the defendant to prove the alternative and its cost. It has been held in this court, for example, that in accounting for profits the burden is on the defendant to prove his costs, and thus establish the net profits from his sales: [citations removed]. Consistently with this fundamental principle, it is equally incumbent upon the defendant to prove his real net profits from using the infringing method by establishing on a balance of probabilities what his costs would have been had he used the most likely non-infringing

alternative method. Therefore, the learned referee was right in law in imposing that burden on the defendant in this case.

Also see Apotex Inc v Merck & Co, 2015 FCA 171 at para 74, 387 DLR (4th) 552 [Lovastatin FCA], and Pfizer v Teva, 2016 FCA 161 at paras 53-66, 400 DLR (4th) 723, where the Court said: "[m]ere possibilities short of probabilities do not suffice" [para 56].

[9] The NIA defence was initially received in Canada with some hesitation perhaps because of the qualified language used in Monsanto Canada Inc v Schmeiser, 2004 SCC 34, [2004] 1 SCR 902. More recently, however, the Federal Court of Appeal has fully endorsed the defence, at least in conceptual terms: see Lovastatin FCA and Apotex Inc v ADIR, 2017 FCA 23, [2017] FCJ No 110 (QL) [Perindopril FCA]. But, as with any legal principle, the real challenge lies in its application to the evidence. This case is no different.

[10] Lovastatin FCA, above, contains a useful discussion of the theory behind the NIA defence and the method of applying it. At its root is the need for a causal link between the infringement and the claimed recovery. Behind the application of the NIA idea is said to lie "robust common sense" about what would and could have happened "but for" the infringement. The following passages from the decision are particularly instructive:

[48] The difficulty with the Judge's approach is that if damages for lost profits are calculated never having regard to an available non-infringing alternative, the patentee will sometimes be better off than it would have been in the absence of infringement. This is so for the following reason. Where a defendant can make and sell a non-infringing alternative, the patent does not confer a complete monopoly on the patent holder. Instead, the patent confers a share of market power upon the patentee. In this circumstance, where, instead of using a non-infringing alternative, a defendant infringes, it is a question of fact whether, "but for" the infringement, the defendant would not have competed with it. The defendant's lawful competition in the "but for" world may have deprived the patentee of some sales.

[49] Put another way, in cases where, in the "but for" world, the infringer could and would have made and sold a non-infringing alternative, these sales may well reduce the patent owner's sales. Awarding the patentee full damages for lost profits in every case will, therefore, sometimes over-compensate the patentee.

[50] Perfect compensation requires consideration of: (i) what, if any, non-infringing product the defendant or any other competitors could and would have sold "but for" the infringement; and, (ii) the extent lawful competition would have reduced the patentee's sales.

...

[73] When considering the effect of legitimate competition from a defendant marketing a non-infringing alternative, a court is required to consider at least the following questions of fact:

i) Is the alleged non-infringing alternative a true substitute and thus a real alternative?

ii) Is the alleged non-infringing alternative a true alternative in the sense of being economically viable?

iii) At the time of infringement, does the infringer have a sufficient supply of the non-infringing alternative to replace the non-infringing sales? Another way of framing this inquiry is could the infringer have sold the non-infringing alternative?

iv) Would the infringer actually have sold the non-infringing alternative?

[74] As a matter of principle, the burden lies on the defendant to establish the factual relevance of a non-infringing alternative on a balance of probabilities. Indeed, Apotex acknowledged in oral argument that it bears the persuasive burden, on a balance of probabilities, to prove that it would have used the non-infringing alternative. This is consistent with jurisprudence such as Rainbow Industrial Caterers Ltd. v. Canadian National Railway Co., [1991] 3 S.C.R. 3, 84 D.L.R. (4th) 291.

[Emphasis in original.]

...

[89] While this is dispositive of the appeal on this issue, I also find that Apotex failed to establish that it would have replaced its infringing sales. I reach this conclusion on the following basis.

[90] First, as Apotex conceded in oral argument:

- The real world informs our construction of the “but for” world.
- Conduct in the real world is “very important” to what would have happened in the “but for” world.
- Findings of fact from the liability decision are relevant to constructing the “but for” world.
- “Brazen” infringement in the real world makes it very difficult to prove that the defendant would have deployed the non-infringing alternative in the “but for” world.

[91] In the liability phase, the Judge found, at paragraph 309 of her reasons (reported at 2010 FC 1265), that if Blue Treasure had been using the non-infringing process to ferment lovastatin, it would have lost significant amounts of money for each kilogram of product it shipped to AFI. However, Apotex knew that once Blue Treasure began to use the allegedly non-infringing process it became profitable. The inference to be drawn is that Apotex knew Blue Treasure was in fact using the infringing process; yet Apotex used that bulk product to prepare and sell its lovastatin tablets.

[92] In this circumstance it is relevant to note that from January 1, 1997 to January 1, 2001 Apotex believed Merck’s patent was invalid.

[93] Apotex' evidence falls far short of demonstrating that it would have sold the non-infringing product when one considers: the scale of Apotex' infringement; its likely knowledge that Blue Treasure was supplying it with infringing lovastatin; its belief the Merck patent was invalid; its failure to call a witness from AFI to support its contention that, had it known the product was infringing, it would have resurrected operations at AFI in Winnipeg; and the fact the Judge found that the testimony of Apotex' only fact witness was, albeit not on this point, unsubstantiated and self-serving.

[11] The NIA defence was more recently endorsed in Perindopril FCA, above. There Apotex advanced the defence based on the asserted availability of the patent-protected product from certain foreign sources for sale into non-infringing markets. The Court expressly rejected the idea that a NIA could not take the exact form of the patented product. Such an approach, it said, would inappropriately extend the territorial reach of the Canadian patent into non-infringing jurisdictions. The Court was also unperturbed by the fact that, at the beginning of the infringing period, none of the identified foreign third-party suppliers of Perindopril had the compound at hand. The question posed was whether, in the hypothetical world, Apotex could and would have obtained sufficient quantities of non-infringing product and that it could and would have used that product [see para 41]. The Court discussed this point in the following way:

[42] As this Court later explained in Pfizer Canada Inc. v. Teva Canada Limited, 2016 FCA 161, 483 N.R. 275, (Effexor) at paragraph 50, both the "could have" and "would have" requirements are important. To prove "could have", the defendant must demonstrate that it was possible for it to secure non-infringing product. To prove "would have", the defendant must demonstrate "that events would transpire in such a way as to put them in that position" (Effexor, paragraph 50). The importance of the "would have" requirement is that by requiring a defendant to show that it would have used a non-infringing alternative, the defendant shows that the value of the patented invention is not such that reliance on alternatives is unlikely or fanciful. Put another way, notwithstanding the availability of a non-infringing alternative, the defendant must show that there are no impediments to its use.

[12] AstraZeneca contends that the jurisprudence does not support a NIA that is not perceived by the infringer to be non-infringing at the point of the infringement. It also posits that a NIA must be "foreseeable" to the infringer at the relevant time. Anything short of this is said to be speculative.

[13] In support of the "knowledge" requirement, AstraZeneca relies on the trial decision in Wellcome Foundation Ltd v Apotex Inc (1998), 82 CPR (3d) 466 at paras 32-33, 151 FTR 250 (FCTD) [Wellcome FC], aff'd [2001] 2 FCR 618, 11 CPR (4th) 218 (CA). AstraZeneca cites to Lovastatin FCA, above, at paras 93-95 on the issue of foreseeability.

[14] I do not read these decisions as broadly as AstraZeneca suggests. In Wellcome FC, above, Justice MacKay did focus on whether Apotex had actual knowledge that its proposed NIA was non-infringing, but he also considered whether "it could have known" [para 33]. Knowing whether or not a proposed NIA would infringe is, of course, a factor in determining whether the infringer "would have" employed it in place of the infringing product. But this falls well short of making prior knowledge of non-infringement an absolute pre-requisite to the assertion of a NIA.

[15] I also place little significance on the stray reference to "foreseeability" in Lovastatin FCA, above. In the context of its use I take that reference to mean only that the concept of a viable NIA would have been available to the infringer based on what was known in the art at the time. If foreseeability meant that the infringer must have the asserted NIA in mind at the time of the infringement, it could potentially punish those who had no idea their product was infringing while rewarding those who had an appreciation of the risk and courted it, but nevertheless had a back-up, work-around solution available.

[16] In its Closing Argument on NIA at para 56, AstraZeneca cites two United States authorities (Grain Processing Corp v American Maize-Products Co, 185 F 3d 1341 (Fed Cir 1999) [Grain Processing], and Micro-Chemical Inc v Lextion Inc, 318 F 3d 1119 (Fed Cir 2003) [Micro-Chemicals]) for the idea that a NIA requiring the infringer to "invent around the patented technology" is not considered to be "available" to the infringer. I do not agree with this interpretation and in oral argument counsel retreated somewhat from the above proposition. Neither Micro-Chemical, above, nor Grain Processing, above, stand for the idea that the availability of a NIA is necessarily contingent on the amount of inventive effort required to make it. The time and effort of coming up with a non-infringing solution is certainly relevant to whether the infringer would have pursued it, but they are not absolute barriers to the defence. That this was all Judge Rader for the Court was saying in Micro-Chemical is clearly evident from his statement at p 1123 that high costs and the complexity of the exercise "to design or invent around the patented technology to develop an alleged substitute weighs [sic] against a finding of availability". The Court in Grain Processing makes the same point.

[17] The American authorities cited by the parties also do not, on my reading, support an argument for exclusion of a NIA that is not "on the market" at the time of infringement. In Grain Processing, above, the Court was only concerned with the hypothetical availability of a NIA "including but not limited to products on the market" [p 1349]. Where the substitute was not on the market at the relevant time, the Court observed that an inference of unavailability could be drawn but not that it must be drawn. The Court went on to say at p 1353 that "the trial court must proceed with caution in assessing proof of the availability of substitutes not actually sold during the period of infringement". In that case, however, the trial court had found that the asserted substitute could have been made by a process that was known in the art. That finding was upheld on appeal. I can see nothing in the Micro-Chemical decision that detracts from the above view.

[18] There is, of course, a difference between cases like Perindopril FCA and this one. In Perindopril FCA the NIA was known to exist at the time of infringement. The NIAs Apotex proposes in this case were unknown and never made by anyone before or during the infringing period let alone approved for use in Canada, the United States or elsewhere. Notwithstanding this distinction, I accept Apotex's point that in the hypothetical, but for pharmaceutical world the infringer's failure to produce a viable NIA formulation in the real world is not a threshold bar to the use of the NIA defence. In this context, the question is: Could the infringer have made the product had it attempted to do so at the relevant time and would the infringer have sold the product on some reasonable financial basis in substitution for the infringing product?

[19] I think this is the point being made by Justice Eleanor R Dawson for the Court in Perindropril FCA, above, when she said at para 62 "the fact that an event does not take place in the real world does not necessarily mean that the event could not and would not have taken place in the hypothetical world". Added to this is the recognition in Perindropril FCA that the availability of a NIA is not to be foreclosed simply because it was not immediately available to the infringer, i.e. on the eve of first infringement. The Court is still obliged "to consider whether at some later point in time a supplier would and could have provided" a replacement product [see para 67]. This lends support to Apotex's view that a viable NIA need not exist at the exact time of infringement.

[20] All of this is not to say that the post-infringement development of a NIA does not present problems of proof for the infringer asserting the defence. Indeed, as explained below, serious problems of proof are manifest in this case.

[21] One of the difficulties with an ex post facto NIA solution was recently discussed in Bell Airbus Helicopters SAS v Bell Helicopter Texteron Canada Limitée, 2017 FC 170 at para 295, 144 CPR (4th) 281 [Airbus]. There Justice Luc Martineau explained that the Court must be very wary of hindsight bias when it considers the claimed ease with which an after-the-fact NIA could be developed, tested, scaled-up and approved for use. In a case where the use of a product carries considerable infringement risk, one is left to wonder why the supposedly simple, non-infringing, equal cost version was never attempted. The "could have and would have" evidentiary concerns are also magnified when the proposed hypothetical NIA(s) were never, at any time, submitted to the relevant regulator for assessment and approval.

[22] I do not, however, think that Justice Martineau's decision in Airbus, above, stands for the proposition that ex post facto NIAs of the sort proposed in this case must be excluded from consideration as a matter of law. Justice Martineau simply expressed reservations about the dangers of relying on a NIA that was either unknown during the period of infringement or had been previously discarded. He was appropriately concerned about the reliability of this type of look-back evidence and the risk of hindsight bias [see para 295].

[23] I have similar concerns to those expressed by Justice Martineau about the NIA evidence presented by Apotex in this case concerning its recently developed in-house NIA formulations.

[24] It is one thing to rely upon a NIA that is known and available for use during the period of infringing activity. It is quite another thing to propose a NIA made long after an infringement has taken place. When a pharmaceutical NIA has been created and has obtained regulatory approval, one is not left to wonder whether it "could" have been available for use (assuming a capacity to obtain it in commercial amounts). In this case, however, Apotex's self-created NIAs were made in non-commercial batches, without full stability, bioequivalency or clinical studies, and without obtaining the required regulatory approvals for commercial use. Indeed, Apotex had no intention of ever developing these formulations for commercial exploitation. Many questions, therefore, remain about whether and, if so, when any of the formulations could have been used successfully during the period of infringement.

[25] Apotex attempts to explain away the evident weaknesses in its testing evidence with the argument that AstraZeneca and its experts misconceived Apotex's NIA burden. Apotex puts the issue in the following way, at para 113 of its Closing Submissions:

...The issue before the Court is whether one or more of the NIA formulations could meet regulatory requirements had Apotex manufactured them at a commercial scale and made the requisite regulatory filings, not whether the data generated is sufficient to meet regulatory standards.

- Were Apotex to have done what Astra requires of it, millions of capsules would have had to be manufactured and studied over the period of a year. Moreover, hundreds of humans would have needlessly been subjected to clinical studies.

[26] The difficulty with the above idea is that, without ever acquiring the data necessary to satisfy regulatory requirements for its proposed NIAs, Apotex cannot directly establish that any of them would have obtained that approval. Incomplete or inconclusive data is weak data. The fact that Apotex began its stability testing too late to get it finished before trial and did not conduct clinical bioequivalency research at all does not make its case for NIA viability any stronger. The same can be said of the experimental short-cuts and less-than-optimum testing protocols employed by Apotex in the generation of its stability data. While these approaches may be entirely appropriate for the purpose of making in-house formulation choices to advance product development, they have diminished probative value where the question is whether a particular formulation would have been sufficiently viable to obtain regulatory approval on a balance of probabilities.

[27] It is also of some significance that Apotex unsuccessfully asserted a NIA defence in the damages-assessment phase of the United States litigation. Apotex argued there that it could have made adjustments to the infringing formulation, adopted an existing non-infringing formulation or used a microtablet formulation. These arguments were wholly rejected by

> the United States District Court for the Southern District of New York [District Court] in AstraZeneca AB v Apotex Corp, 985 F Supp 2d 452 (2013). The Court characterized Apotex's proposed formulation adjustments in the following way, at p 499:

As for Apotex's proposals for tinkering with the ingredients in its pellets, it is pure speculation whether any of its various proposals would create a stable, bioequivalent product that was non-infringing. Apotex has never asked one of its many experts to try to create the revised formulation, much less to create and test it. See SynQor, Inc. v. Artesyn Techs., Inc., 709 F.3d 1365, 1382 (Fed.Cir.2013) (where an alleged substitute is not on the market, "the accused infringer has the burden to overcome the inference that the substitute was not 'available'") (citation omitted).

There is a reason that Apotex chose the ingredients that it did for its pellets following six years of research and testing. Those ingredients created a successful product. This is no easy task given the challenges of working with the omeprazole molecule and delivering it sufficiently intact to the part of the body in which it is most effective.

[28] In this case, Apotex belatedly attempted to overcome the problem identified by the District Court by developing a set of alternative formulations. However, Apotex has not adequately explained why it waited until late 2015 to begin its stability testing when it knew or ought to have known as of 2007 from the United States litigation that Apo-Omeprazole infringed AstraZeneca's formulation patents. Inexplicably, Apotex mounted a purely theoretical NIA posture in the damages-assessment phase of the United States proceeding and by the end of that case, the Court observed at p 449 that it had "largely abandoned its argument that it could have altered the infringing formulation successfully". The rejection by the District Court of Apotex's NIA defence was based on a different and presumably weaker evidentiary record than the record before me. Nevertheless, I am left to wonder why Apotex failed to work-up its asserted alternative formulations in this case long before the end of 2015. Its excuse that it thought its formulation was non-infringing is undermined by the 2007 District Court finding of infringement [see AstraZeneca AB v Mylan Labs Inc et al, 490 F Supp 2d 381 (2007)] which was subsequently upheld on appeal in 2008 in AstraZeneca AB v Apotex Corp, 536 F 3d 1361 (Fed Cir). Apotex's stability testing thus commenced long after it knew or ought to have known that Apo-Omeprazole was infringing.

[29] Apotex's failure to complete the testing of its alternative formulations and to instead rely on extrapolations from its experts in this case is an unacceptable approach. A recognition of this strategy would potentially reward Apotex for its delay by excluding from consideration finished stability test results – data that may well have established that the alternative formulations would not work. It cannot be to Apotex's advantage that its delay in the initiation of obvious testing avoids the potential for failed results. What Apotex is asking is that the Court predict a result that it could have but failed to establish. On the evidentiary record before me, I am not prepared to draw the inferences Apotex is seeking.

[30] AstraZeneca relies heavily on the principle that in the assessment of the but for world of NIAs the Court must look at what took place in the real world including the behaviour and state of mind of the infringer. Apotex does not deny this as a point of principle but argues for its reduced significance.

[31] Initially I did have reservations about the idea that the availability of a NIA can be informed, in part, by the willfulness of the infringement. But as I understand the decision of the Federal Court of Appeal in Lovastatin FCA, the idea is no more than this: where an infringer brazenly infringes a valid patent, or substantially courts the risk of doing so, an inference may arise that no viable substitute was available. If it were otherwise the rational choice would always be to employ the NIA and not the infringing product.

[32] It seems to me that what Apotex knew at the time and what it did in response to that knowledge in the real world are important considerations in the assessment of the hypothetical availability of its after-the-fact NIAs. The suggestion today that the development and commercial exploitation of the asserted NIAs would have been simple, cost-effective and speedy is substantially belied by historical fact.

[33] It is worth noting that it took Apotex many years to develop and obtain regulatory approval for Apo-Omeprazole – a product that Dr. Bernard Sherman apparently thought at the time would not infringe the 693 Patent or the United States 505 Patent. This fact belies the argument that any of the NIAs would have enjoyed an easier route to success if they were developed from scratch and without the benefit of the development of Apo-Omeprazole. Indeed, as I found in the liability phase, omeprazole is not an easy molecule to formulate.

[34] Dr. Sherman's evidence that a work-around NIA solution was a straight forward task is also belied by the experience of producing the now-asserted NIA formulations. Initially Dr. Sherman thought the solution lay in the removal of the alkaline reacting compound [ARC] from the infringing formulation. Indeed, that was Dr. Sherman's evidence in the United States litigation. However when that approach was adopted for this proceeding, it failed [see Exhibit APO 130, Chow Report #1 at paras 84-85].

[35] It is also noteworthy that none of the first 14 NIA formulations produced by Apotex were pursued in this litigation. This supports an inference that each of them failed. Of those formulations that did go forward to further testing, a number clearly failed to meet the necessary stability or bioequivalency requirements. Of those formulations that Apotex continues to assert, several were developed later in the selection process. All of this undermines Apotex's argument that numerous viable NIA options would have been immediately obvious to a skilled formulator like Dr. Sherman.

[36] Dr. Sherman's excuse for not exploring his NIA options during the infringing period was that he had no reason to think Apo-Omeprazole was infringing. This evidence does not stand up to scrutiny. Indeed, as discussed above, it either was or should have been increasingly obvious to Dr. Sherman that Apo-Omeprazole was likely an infringing product. Notwithstanding what Apotex knew or ought to have known, it persisted with its use of Apo-

Omeprazole. This continued infringing conduct was unreasonably stubborn or dogmatic, if not wilfully blind to the consequences, and it contradicts Dr. Sherman's trial testimony that, had he known, Apotex would have immediately searched for other options.

[37] It is also of some significance that despite increasing evidence of infringement Apotex chose not to examine Apo-Omeprazole to determine if it incorporated an infringing subcoat. All of this conduct undermines Dr. Sherman's evidence that if he had only known Apo-Omeprazole was infringing, he could easily have developed or purchased a NIA. The more sustainable inference is that Apotex was prepared to run with Apo-Omeprazole whatever the likely consequences and it is doubtful it would ever have pursued a NIA option. That is particularly the case for pursuing a third-party NIA. Dr. Sherman made it very clear that such an approach would not have been considered unless and until he had exhausted his in-house options.

[38] In assessing Dr. Sherman's evidence about what Apotex would have done in the hypothetical world it is necessary to consider what he knew in the real world and what Apotex did or did not do with that knowledge.

[39] At least as early as 2000, Apotex knew that AstraZeneca was asserting an infringement allegation based on an in situ formed subcoat in connection with another generic omeprazole formulation. In AB Hassle et al v Canada et al, 10 CPR (4th) 38, 102 ACWS (3d) 185 (FC), aff'd 2002 FCA 147, 18 CPR (4th) 558, Justice Daniele Tremblay-Lamer made a finding of infringement on that basis.

[40] In 2000, AstraZeneca made the same allegation against Apotex and other generics in the infringement action in the United States. In the first wave of that litigation, concluded in 2002, the District Court found infringement on the part of a different defendant for an in situ formed subcoat. At the conclusion of the second wave of cases in 2007, discussed above, the same finding was made against Apotex.

[41] In 2003, the Federal Court of Appeal construed the 693 Patent claims to cover an in situ formed subcoat and rejected Apotex's arguments to the contrary: see AB Hassle v Apotex Inc, 2003 FCA 409, 29 CPR (4th) 23.

[42] In 2004, AstraZeneca commenced the first of these proceedings in Canada against Apotex for damages, alleging again that Apo-Omeprazole infringed the 693 Patent on the basis of an in situ formed subcoat.

[43] Notwithstanding the above history, Apotex took no steps to pursue a NIA formulation or even to test whether Apo-Omeprazole capsules contained an infringing subcoat layer.

[44] On March 16, 2015, I rendered a Judgment in these proceedings finding Apo-Omeprazole to be infringing of the 693 patent because it incorporated a sub-coat layer formed in situ.

[45] Having regard to the above background and to the fact that no effort was made by Apotex until late 2015 to develop any NIA formulations nor at any time or to pursue a third-party formulation, considerable caution is warranted.

[46] Apotex had no readily available NIA options at any time during the infringing period and it had no back-up plan to develop or purchase one. Instead it ran with Apo-Omeprazole to the end. Even now Apotex produced late, incomplete and inconclusive stability and bioequivalency data suggesting that it did not, and to this day does not, have a viable in-house NIA option. Notwithstanding these concerns, I will proceed with an assessment of Apotex's evidence concerning its asserted NIAs to determine whether they were available and true non-infringing substitutes for Apo-Omeprazole.

[47] In that regard I can readily dispose of two issues raised by AstraZeneca:

(a) whether Apotex had the capacity to commercialize one of its asserted NIA formulations (the could-have question); and

(b) whether Apotex has failed to prove that each of its asserted in-house NIAs is non-infringing.

[48] While I accept that there would be manufacturing challenges for Apotex during scale-up to commercial NIA production, I believe that, with the exception of NIA formulation MR8620E1, these could be overcome by a successful and sophisticated producer like Apotex. Enteric coatings have been commercially used for many years and Apotex had considerable experience in successfully applying them to its formulations. Dr. Davies identified a number of production obstacles that Apotex may not have fully resolved in its small-scale batches. However, I am left with the impression that Apotex could and would have resolved most of these issues without the inordinate expenditure of time or money and without compromising the dissolution profile of the enteric coatings used in the NIA formulations.

[49] I exclude from this finding formulation MR8620E1. That formulation was designed to avoid an in situ subcoat by reducing the water content of the MACP enteric coating dispersion. This change reduced the potential for a reaction at the enteric coating/core interface.

[50] I am not satisfied that MR8620E1 could have been commercially developed because, as Dr. Davies explained, it failed to meet the MACP manufacturer's specification for solids content and this repeatedly caused nozzle blockages [see Exhibit AZ 137 at paras 136-37]. In the absence of persuasive evidence proving that this production problem could be overcome at commercial production levels, I am not convinced that it would have worked. Indeed, if it was as obvious a work-around as Apotex now suggests, one is left to wonder why it was not attempted until well into Apotex's NIA development and why larger scale enteric coated batches were either not attempted or were left undocumented.

[51] I am also satisfied on the evidence provided by the Apotex witnesses that it had ample in-house capacity to produce the remaining NIA formulations, sufficient to match its infringing sales.

[52] AstraZeneca contends that Apotex has failed to prove that its proposed NIAs would not infringe the 693 Patent. Although AstraZeneca has stipulated that Apotex's proposed NIAs produced at batch scale do not infringe [see Exhibit APO 69], it does not concede the same point for any of the NIAs if produced at a commercial scale. I do not accept this argument because it lacks direct evidentiary support.

[53] If the NIAs are non-infringing at batch scale, one would expect them to remain non-infringing on commercial scale-up. That expectation might be rebuttable with cogent evidence that a production scale-up would be likely to give rise to an infringing characteristic (e.g. an in situ subcoat layer). No evidence directly on point was before me and I find that the asserted NIA formulations at commercial scale would not infringe the 693 Patent.

A. Are the Proposed NIAs Bioequivalent to LOSEC? [54] Dr. Mario González is an expert in pharmacokinetics, clinical pharmacology and biopharmaceutics [including the development and application of in vitro–in vivo correlations and relationship in predicting bioequivalence of formulations]. He provided expert opinion evidence on behalf of Apotex as to whether, in the absence of in vivo data, one could reasonably predict that any of the asserted NIAs would be likely to be bioequivalent to LOSEC and, if so, how the prediction could be made.

[55] After advising Apotex that, in certain circumstances, such predictions could be made, Apotex gave Dr. González its pharmacokinetic/statistical clinical data comparing the bioequivalency of Apo-Omeprazole and LOSEC along with its in vitro dissolution data and testing protocol. From that information Dr. González was asked to provide an opinion "as to whether any of the [NIAs] would be expected to be bioequivalent to Losec".

[56] Dr. González's first report [see Exhibit APO 41] acknowledges that assessing bioequivalency for regulatory purposes between two pharmaceutical compounds is carried out with randomized, cross-over human clinical testing where blood plasma concentrations are measured over time and compared. Acceptable clinical studies would require at least 12 human subjects but more typically between 18 to 24 subjects "to gain meaningful data". The tested population needs to be large enough such that the data are not unduly thrown-off by intra- and inter-subject variability. Health Canada will accept two formulations as bioequivalent if the comparative data meet minimum statistical standards [see para 32].

[57] Dr. González's first report states, at para 33:

where it is undesirable or impractical to conduct a comparative bioavailability study to determine whether two formulations are bioequivalent, it is, in certain circumstances, possible to use alternative methods, such as an in vitro/in vivo correlation ("IVIVC") or an in vitro/in vivo relationship ("IVIVR"), to provide a reasonable prediction that two formulations will be bioequivalent.

[58] In this case an IVIVC could not be carried out and Dr. González was limited to using the less robust IVIVR method – a technique that he said "can be of great value during formulation development" [see para 38].

[59] Dr. González began his IVIVR bioequivalency work-up by plotting the bioequivalency data for Apo-Omeprazole and LOSEC. He observed them to be bioequivalent in the fasted state. According to Dr. González any NIA formulation with an in vitro dissolution profile that fell between those of Apo-Omeprazole and LOSEC "would be expected to be bioequivalent to these formulations" [see para 52]. Such a prediction could not be made with the same degree of confidence for a NIA with an out-of-range profile. Of the fifteen NIA formulations Dr. González examined, eight fell within the Apo-Omeprazole and LOSEC dissolution profiles. The others were said to be "less likely to be bioequivalent to Losec® and Apo-Omeprazole based on dissolution data" [see para 60]. Dr. González then carried out a comparison using the f2 metric for similarity for the remaining eight NIA formulations and observed them to be similar to either LOSEC or Apo-Omeprazole. He concluded that all eight "would be expected to be bioequivalent to Losec® and Apo-Omeprazole" [see para 65].

[60] AstraZeneca countered Dr. González's evidence with the opinion of Dr. David Taft. He was qualified as an expert in pharmaceutical sciences, including pharmacokinetics.

[61] Dr. Taft was asked to advise if IVIVR was an accepted and reliable technique for predicting bioequivalency generally and, more specifically, for predicting the bioequivalency of the Apotex NIAs to LOSEC or Apo-Omeprazole based on the available data.

[62] Dr. Taft defined bioequivalency and its regulatory significance in the following way in his responding report [Exhibit AZ 160]:

37. Bioequivalence has been defined as, "the absence of a significant difference in the rate and extent to which the active ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study." (emphasis added)

38. Government agencies that regulate marketed drugs, like the FDA and HC, set standards for how "absence of a significant difference in the rate and extent" are to be determined. Cmax and AUC are the parameters used to measure the rate and extent of absorption.

[Emphasis in original.] [Footnotes omitted.]

[63] Dr. Taft expressed the opinion that the bioequivalency of LOSEC and Apo-Omeprazole was not established by the data relied upon by Dr. González. He was particularly concerned by the exclusion of data from one of the test subjects (OM75). Had those data been included, the results of the Apotex study would not have satisfied either the Health Canada or the United States Food and Drug Administration [FDA] requirements for bioequivalency. Notwithstanding Dr. Taft's concern, the fact remains that regulatory approval was obtained for Apo-Omeprazole and presumably the exclusion of OM75 was accepted by the regulators.

On the evidence presented, including Dr. Taft's evidence at Transcript p 4087 and Exhibit AZ 78, I am not prepared to look behind that decision to reassess its scientific merit.

[64] Dr. Taft was highly critical of Dr. González's analysis for other reasons. He challenged Dr. González's use of mean dissolution and absorption data obtained from the Apotex Apo-Omeprazole biostudy based on the wide variability of the actual plasma concentrations for each of the test subjects as compared to the mean. Figure 6 of his report, at p 31, nicely depicts this variability. According to Dr. Taft this variability weakens the IVIVR model as a foundation for comparing LOSEC and Apo-Omeprazole to the NIAs.

[65] According to Dr. Taft, the problem of subject-to-subject variability in the Apotex biostudy data for Apo-Omeprazole is compounded by the variability in the in vitro dissolution data for the NIAs used by Dr. González. Because all of the dissolution data for the NIAs exceeded the accepted margin of 10% for the IVIVC method, the data, he thought, were "too variable to use for reliably predicting bioequivalence" using the less robust IVIVR method [see para 116].

[66] Dr. Taft was also critical of Dr. González's use of IVIVR as a predictive tool in proof of bioequivalence. He pointed out that IVIVR is only useful as a tool for guiding formulation development. According to Dr. Taft, there is nothing in the literature supporting its reliability for predicting bioequivalence or indicating that it can be used as a substitute for an IVIVC. Furthermore, Dr. González's IVIVR method did not meet the minimum standards required of an IVIVC. Dr. Taft concluded this part of his report in the following way:

126. More fundamentally, Dr. González's "IVIVR" technique is incompatible with the underlying principles for an IVIVC. An IVIVC is based on a formulation consistently demonstrating a relationship between in vitro dissolution and in vivo absorption. Dr. González's "IVIVR" is based on an entirely different proposition. In particular, Dr. González's "IVIVR" technique contends that where different formulations with different in vitro dissolution profiles (i.e., Apo-Omeprazole and LOSEC) have similar in vivo absorption profiles, any test formulation (i.e., an AF) that has an in vitro dissolution profile lying between the other two will also have the same in vivo absorption profile (and hence be bioequivalent). That is, as he seems to acknowledge, Dr. González's "IVIVR" technique is not based on a correlation between in vitro dissolution and in vivo absorption; but rather on the assumption that such a correlation is irrelevant. However, if dissolution is irrelevant to absorption, then it is not predictive of absorption.

127. Based on the foregoing, in my view the scientific community has not accepted and would be unwilling to accept Dr. González's "IVIVR" technique for establishing bioequivalence of the [NIAs] to Apo-Omeprazole or LOSEC.

[Footnotes omitted.]

[67] Dr. Taft had several other concerns about Dr. González's use of IVIVR to predict the bioequivalence of the NIAs to LOSEC and Apo-Omeprazole. These included his failure to estimate the error rate, the lack of validation as required by the FDA for IVIVCs and the lack of any data showing bioequivalence in the fed state.

[68] Dr. González's reply report generally addressed the points advanced by Dr. Taft [see Exhibit APO 43]. In particular, he picked up on Dr. Taft's point that LOSEC and Apo-Omeprazole exhibited different dissolution rates for the first 40 minutes. When Dr. González adjusted for the five minute time lag in dissolution between the two formulations, the profiles were similar.

[69] Dr. González commented on Dr. Taft's view that some in vivo absorption data for the NIAs was needed for a valid IVIVR. Dr. Taft's point was weakly countered with the following statement, at para 45: "[h]owever, if there were in vivo data available for these formulations, this would remove the need for an IVIVR". Dr. González's substantive response was limited to the observation that, as "minor" variations to Apo-Omeprazole, the NIAs would be assumed to have the same linear relationship between dissolution and absorption.

[70] Dr. González accepted that "there may be some larger than expected variance" in the dissolution data for the NIA formulations. This he attributed to the fact that the NIAs came from pilot scale batches "as opposed to optimized formulations" but "this does not mean that the data are unsuitable for use in an IVIVR" [see para 57].

[71] Dr. González answered Dr. Taft's concern about the IVIVR technique not being peer-reviewed or generally accepted in the scientific community in the following way:

58. At paragraphs 118 to 127 of his report, Dr. Taft provides the opinion that the IVIVR technique that I used in my prior report was not peer-reviewed or generally accepted. However, I know from my personal experience in the pharmaceutical industry that, while IVIVRs may not be the subject of large numbers of journal articles, IVIVRs are routinely used within the pharmaceutical industry, and have been used since the early 1980s during formulation development to direct the modification of formulations. An IVIVR allows a formulator to decide if a modified formulation is likely to be successful in a bioavailability study, and thus whether to test in a human population.

59. During formulation development, it would be rare for an IVIVC to be available for an early formulation, and it is not practical to conduct an in vivo bioavailability study for each formulation prepared during the development of a product. Rather, in vivo data will only be obtained for a select number of formulations, and an IVIVR will be used to identify a bio-relevant dissolution test to identify additional formulations that would be expected to be bioequivalent to, or to have a better drug absorption profile, for example, a longer tmax than, a reference formulation.

[72] Dr. González's reply also took issue with Dr. Taft's application to the IVIVR model of a 10% prediction error threshold used in IVIVCs. His less than compelling response was that the IVIVR model would be expected to throw off a higher error rate than an IVIVC such that "a prediction error of 10-20% [would] be good for an IVIVR". He summed up the point in the following way:

73. For these reasons, it is not at all surprising that an estimate of prediction errors with an IVIVR would differ from those typically seen with a more rigorous and robust IVIVC. The intent of an IVIVR is to provide assurance of the likely performance or bioequivalence of a test formulation when compared to a reference formulation without requiring the need for larger amounts of in vivo data, and also allowing for a greater range of differences between formulations.

[73] Dr. González responded to the absence of NIA bioequivalence data in the fed state by pointing out that because Apo-Omeprazole is bioequivalent to LOSEC in the fed state, and because the NIA formulations were similar to LOSEC and Apo-Omeprazole, the NIAs would also be expected to be bioequivalent in the fed state.

[74] Under cross-examination Dr. González accepted that the best means of establishing bioequivalence is through a well-designed clinical study [Transcript p 1235]. Dr. González also stated that one does not "run a bio study with some little pilot formulation. You want to make sure that you have a really good formulation before you get into a bio study" [Transcript p 1241].

[75] Dr. González was questioned closely on his view that, because the NIA formulations were similar to LOSEC and Apo-Omeprazole, they would be expected to behave in the same way. He conceded that he was not a drug formulator and he was clearly out of his depth with respect to this issue, as can be seen from the following exchange at Transcript p 1307:

Q. Moving away from the compression forces to the ingredients: In your view, these formulations are similar because they have the same ingredients?

A. Yes. Omeprazole, mannitol, magnesium hydroxide and povidone, yes.

Q. Let's look at the first experimental formulation, 15-1214B. That doesn't have magnesium hydroxide. It doesn't have povidone?

A. That is true.

Q. Let's look at the third one.

A. Qualitatively, that one is different.

Q. The third one, that is different too. Fifteen -- I think it should read "12"?

A. Povidone is missing.

Q. Next one, the ingredient is missing?

A. "Magnesium hydroxide" is missing. Right.

Q. Next one, an ingredient is missing?

A. That is true.

Q. Next one, as well, 6108-288C. So many of these formulations do not have the same ingredients. Correct?

A. That is true, but I am not using any of these formulations to arrive at the IVIVR. I am using the dissolution profiles from these formulations to see how well they fall within the other two dissolution profiles.

Q. You just said, Dr. González, that you were relying on the ingredients being the same to assume that they would have the same relationship.

A. Yes, I did say that.

Q. So you can't make that assumption?

A. Not for all of these formulations, no. On the next page, the other four all do have the same ingredients and, in fact, even the same percentage, so I don't know how --

[76] Dr. González was asked about the differences between IVIVCs and IVIVRs. He referred to the IVIVC as “a predictive mathematical model” and conceded that the IVIVR “doesn’t have such clout” [Transcript p 1313]. The IVIVR is less reliable in predicting bioequivalence [Transcript p 1315]. Unlike the quantitative information produced by an IVIVC, the IVIVR shows only a “qualitative” relationship [Transcript pp 1314, 1320-21]. Establishing an IVIVR would not be accepted by a regulator as evidence of bioequivalence because it does not produce the required quantitative data [Transcript p 1321]. Rather, IVIVRs are typically used as a directional screening tools to guide formulation development. They are not a replacement for biostudies [Transcript pp 1355-56].

[77] The predictive value of an IVIVR was further explained by Dr. González in the following exchange at Transcript p 1359:

Q. But you didn't have a biostudy for a single one of the experimental batches?

A. No.

Q. Do you agree with Devane and Butler that in vivo data for the experimental batches would permit a reality check on your IVIVR model?

A. Well, I would agree that at some point in time, Apotex would eventually run a biostudy on one or two of those formulations. But that it needs to be done for them to select a formulation to pursue, I don't think you have to run a biostudy at that stage.

[78] In another exchange Dr. González refused to accept a characterization by Devane and Butler that IVIVRs have “limited value”. He answered by saying that IVIVRs produce “some predictive value, that your dissolution shows a relationship to in vivo absorption” [Transcript p 1361]. Even in the absence of biostudy data for the NIA formulations, Dr. González expressed the opinion that “there is a good chance that they are bioequivalent” [Transcript p 1370] and “[s]ome of them appear to be bioequivalent on the basis of IVIVR or should be bioequivalent on the basis – of the fact that their dissolution falls within the dissolution of the product that we are testing” [Transcript p 1371]. And further at Transcript pp 1372 and 1378, he stated:

We have a set of two dissolution profiles. Now I have a bunch of formulations that have a similar mechanism of release or at least what I assume is a similar mechanism of release. There is a good chance those are going to fall -- that the ones to fall within the two dissolution profiles will have a good chance for bioequivalence. That is it.

...

That is exactly what I did actually. I took two extreme batches that were bioequivalent, and now I am hoping that these other ones will fall in there, that they are going to be clinically relevant.

[Emphasis added.]

[79] Generally speaking Dr. Taft was a better witness than Dr. González and he provided more reliable evidence on the central issue of the validity of Dr. González’s IVIVR bioequivalency analysis. I would add to this that many of the central aspects of Dr. Taft’s written opinion and his evidence in Chief were left unchallenged on cross-examination. Furthermore, some of the issues addressed in Dr. Taft’s responding report were not answered in Dr. González’s reply. The failure to fully engage with Dr. Taft’s opinions supports an inference that his unchallenged evidence was unimpeachable.

[80] By way of example, Dr. Taft was concerned about the high variability in the Apotex biostudy data for Apo-Omeprazole (what he called a “wide dispersion” of data around the mean result). According to Dr. Taft, data variability is an important factor in the establishment of a valid IVIVR. He addressed this point at Transcript p 4033:

Q. Going back in your report, paragraph 106, given those features, what does that tell you about the reliability of using that data to try to generate an IVIVR?

A. Again, as I have mentioned in paragraph 105, according to Cardot and Davit, in that situation where the mean curve does not reflect the individual behaviour, IVIVC is not recommended. In that context and looking at what we just talked about of the relative data from the OMCP10 that seems to match what is being described by Cardot and Davit, it is my opinion that using an IVIVR based upon biostudy OMCP10 to predict bioequivalence is unreliable.

JUSTICE BARNES: Does it matter that what Dr. González was looking at was not an IVIVC but rather than IVIVR? Does that change anything? And if so, how?

THE WITNESS: In my opinion -- I believe this is the opinion the scientific community -- the only surrogate bioequivalence is a level A IVIVC. You have asked me the question. Essentially, what Dr. González, in my opinion, is attempting to do is to use an IVIVR as if it was a level A IVIVC.

[81] Dr. Taft also spoke to the problem of variability of subject data and the corresponding potential for error in relying on the mean to support an IVIVR. According to Dr. Taft the variability of the data called into question the reliability of the mean as a measure of absorption or dissolution [see Transcript p 4036].

[82] On the issue of using IVIVR generally to predict bioequivalence, Dr. Taft testified as follows at Transcript p 4044:

Q. Turning to the next point, this is more broadly to the extent that that technique has been generally accepted in the scientific community for establishing bioequivalence. What are your views there?

A. In the first case, for example, if it is not available in the peer-reviewed literature, you can certainly look towards regulatory agencies and their opinions and views through guidances and other things.

In the documents that I have reviewed not only in this case but in my day-to-day professional activities, I have never come across a guidance document that would support using an IVIVR to establish bioequivalence of alternate formulations.

[83] It is of some significance that in answer to questions from me, Dr. Taft attributed some value to the IVIVR technique but only as a rough screening tool [Transcript p 4045]:

JUSTICE BARNES: Before you go there, to run this to ground a little bit, it strikes me from what I have heard so far that IVIVR is a "recognized technique," if I could put it that way, in the pharmacokinetic world. It has some value in some places.

THE WITNESS: Yes, Your Honour, it does.

JUSTICE BARNES: Yes, so it is recognized as providing some scientific value to some sort of an analysis. Where does it fit in the scheme of things then?

THE WITNESS: I believe that the Devane paper provided some background on the use of IVIVR in formulation development. Certainly formulators will attempt to rely upon in vitro data to establish or to move products forward in screening. It is not unlike what I do in my day-to-day activities, looking at in vitro pharmacokinetic parameters and relating them to in vivo.

The issue really becomes, in the case of using an IVIVR, to establish bioequivalence. That is, in my view, a totally different application that essentially what you are attempting to do is use the principals [sic] of a level A IVIVC to make that determination, and that is my point.

[84] This evidence is not materially different from Dr. González's ultimate trial testimony.

[85] Dr. Taft went on to calculate the internal prediction error rate associated with Dr. González's IVIVR techniques – a form of validation Dr. González failed to employ. Dr. Taft found a prediction error range between 18.7% and 36.6% – well beyond the validation threshold of 10 to 15%. This led Dr. Taft to reasonably conclude that Dr. González's IVIVR model, based on mean data, was not able to capture the predicted profiles for the test subjects [Transcript p 4052].

[86] Dr. Taft repeated his point that an IVIVR model cannot be used to predict bioequivalency in the fasted state let alone the fed state [Transcript pp 4052-53]. On this issue, I agree with Dr. Taft that a prediction of bioequivalency in the fed state cannot be extrapolated from data observed in the fasted state. Dr. González had no data to support his opinion. That opinion rested only on an assumption that the NIA formulations were sufficiently similar to LOSEC and to Apo-Omeprazole that the ingestion of food would not make any difference to their bioequivalency. The firmness of that view wavered under cross-examination where Dr. González conceded the difficulty of predicting food-effects on formulation bio-availability. He ended with the equivocal statement that one "may be able to predict how things are going to work out" [Transcript p 1327].

[87] The far better evidence on this point came from Dr. Taft. He described the problem of predicting bioequivalency in the absence of a biostudy in the fed state. The presence of food in the stomach, he said, can "influence the absorption of a drug or drug formulation, particularly for an enteric-coated product" [Transcript p 4000; see also Transcript pp 4052-53]. This evidence was not challenged under cross-examination.

[88] Apotex's failure or inability to conduct NIA biostudies in the fed state represents a large gap in its case for bioequivalency. That is so because, if Health Canada required bioequivalency data for any of the NIAs, biostudies in the fed and fasted state would have been necessary just as they were for Apo-Omeprazole [see Exhibit AZ 158 at p 1].

[89] Dr. González failed to counter much of Dr. Taft's evidence about the validity of Dr. González's methods. I accept Dr. Taft's concerns about the variability of the data employed by Dr. González and the corresponding potential for error. Dr. González should also have run a validity analysis of his own and I reject Apotex's criticisms of Dr. Taft's approach to that issue. I also agree with Dr. Taft that the error range for Dr. González's analysis exceeded acceptable levels.

[90] The above-noted methodological problems are sufficient on their own to wholly undermine Dr. González's prediction of NIA bioequivalency. But there is a more fundamental problem with Dr. González's use of IVIVR as a predictive tool – a problem that Dr. González acknowledged up to a point. In his trial testimony Dr. González retreated somewhat from his firmer written opinion.

[91] In his first report Dr. González concluded that eight of the Apotex NIA formulations "would be expected to be bioequivalent to Losec® and Apo-Omeprazole" [Exhibit APO 42, para 65]. However under cross-examination, he conceded that IVIVR is a directional or screening

methodology that only showed the selected NIAs to "have a good chance for bioequivalence" [Transcript p 1372]. Given the inherent limitations of IVIVR as described by Dr. Taft, I reject the suggestion that the IVIVR analysis carried out by Dr. González supports a balance of probabilities finding of bioequivalency. Indeed, the technique in its present form has only a limited value in the area of pre-formulation selection or screening. It produces nothing of quantitative value and Apotex's attempt to extend its reach is unjustified. In these circumstances Dr. González's bioequivalency opinion does not rise above the level of speculation. It is certainly a wholly inadequate proxy for the kind of data required for establishing NIA bioequivalency necessary for regulatory approval. Furthermore, it is an unreliable platform for drawing an inference of bioequivalency. In the result, I find that Apotex has failed to establish that the NIA formulations assessed by Dr. González are, or would be seen by a regulator to be, bioequivalent to either LOSEC or Apo-Omeprazole.

II. Could Apotex Have Conducted Human Clinical Trials on its Proposed NIAs to Prove Bioequivalency? [92] Apotex contends that it could not conduct human clinical trials for its proposed NIAs on ethical grounds. According to this view, because the NIAs were only developed for litigation and no potential health benefits would result, the risks to human subjects would always outweigh the parochial objectives of the work. AstraZeneca disagrees and argues that human clinical trials could have been conducted. AstraZeneca also says that Apotex should, at a minimum, have sought permission from its research ethics board to conduct these studies. By failing to even ask, Apotex failed to produce definitive evidence on the point and should not be the beneficiary of any lingering doubt. Whatever the outcome, the issue, AstraZeneca says, would be conclusively resolved, rendering any ex post facto ethics opinion on the point effectively moot.

[93] Each party called an eminent ethicist in support of its position. Apotex relied on the evidence of Dr. Michael McDonald and AstraZeneca presented evidence from Dr. Charles Weijer. Dr. McDonald testified that a properly qualified research ethics board would not have authorized human clinical studies in these circumstances. Dr. Weijer came to the opposite conclusion.

[94] There is some attractiveness to AstraZeneca's argument that opinion evidence on this issue ought to be excluded in the absence of a research ethics board ruling. I am not convinced, however, that AstraZeneca's suggested approach would necessarily have resolved the matter – at least if the answer provided by the Apotex research ethics board was in the negative. In that event it would remain open to AstraZeneca to argue that the decision was self-serving or wrong. In short, a fact-based negative ruling was unlikely to be a complete and final answer to the question of the propriety of conducting human trials. That is not to say, however, that the approach asserted by AstraZeneca would not have been helpful in determining whether the administration of the Apotex NIA formulations to humans would be unethical and would never be authorized. An actual decision on-point would certainly have provided relevant and likely probative evidence.

[95] I do not accept Dr. McDonald's point that Apotex would have been ethically constrained from even asking its research ethics board if a biostudy could be carried out. Dr. McDonald testified that the circumstances of this case were novel and he posed the question: "how does one deal with a novel case?" [Transcript p 2517]. In the absence of clear guidelines and where there are opposing views about the standards of ethical review to be applied, it cannot be the case that Apotex is entitled to make a pre-emptive and potentially self-serving decision not to approach its research ethics board for direction. Apotex could and should have sought direction from its research ethics board in this case.

[96] It does, however, seem doubtful that Apotex would have been authorized to conduct human biostudies in connection with its hypothetical NIAs, given that the sole purpose of the experiments would be to advance Apotex's litigation interests.

[97] For this, I accept Dr. McDonald's views over those expressed by Dr. Weijer. In particular, I accept Dr. McDonald's evidence concerning the risk-benefit ratio and the ethical requirement that the importance of a research objective outweigh the risks faced by the research subjects. In the case of the Apotex NIAs the risks may have been slight but they were not unworthy of consideration and concern. Where the only benefit of the trials would be to further Apotex's business interests (in contrast to a public good), it is doubtful that ethical approval could have been obtained.

[98] I also disagree with Dr. Weijer that a biostudy involving the human ingestion of an unapproved drug carrying anticipated risks and side-effects and done solely for private commercial or litigation purposes ought to the subject of less rigorous standards or some form of diminished risk-benefit analysis. His idea that there is an underlying public interest in the outcome of private litigation has no appeal. Courts of law decide cases on the basis of available evidence and, in many cases, the evidentiary record is incomplete. It is inconceivable that any Court could or would ever order a litigant to conduct human testing to answer a question relevant to the outcome of a case. At most, an adverse inference can be drawn where a party fails to advance evidence that is potentially available to it.

[99] The fact that Apotex probably could not ethically conduct human bioequivalency studies to prove the efficacy of its unapproved NIAs does not, however, assist it in advancing its substantive case. At most this barrier to human testing prevents the Court from drawing an adverse inference. Human bioequivalency studies are an important means to prove the viability of a NIA and are often required for obtaining regulatory approval. The indisputable fact remains that those tests were not done, leaving a significant gap in the evidence as to whether any of Apotex's NIAs could have been shown to be bioequivalent to LOSEC or Apo-Omeprazole and approved for sale in Canada or the United States.

A. Are the Proposed NIAs Sufficiently Stable? [100] Apotex contends that its testing data are sufficient to meet its burden of establishing that the asserted NIAs were commercially viable substitutes for Apo-Omeprazole. One of the key requirements for proving that viability concerns the stability of those formulations (i.e., did they have an acceptable shelf-life both from a regulatory and commercial standpoint?).

[101] Apotex's stability case was based on data it obtained from in-house stability testing commenced in late 2015, as interpreted by Dr. Kwok Chow. Dr. Chow was accepted as an expert in pharmaceutical product development and drug delivery systems including the design, execution and management of formulation screening, including with respect to the physical and chemical properties of drug substances and excipients, including, specifically, stability thereof.

[102] Dr. Chow was asked by Apotex to review its in-house stability test data for fifteen NIA formulations to determine if they would be expected to have sufficient stability to be useful as pharmaceutical products.

[103] Dr. Chow confirmed in his first report dated September 16, 2016 [Exhibit APO 130] that in-house stability testing of the sort conducted by Apotex is usually done under the research conditions recommended by the appropriate regulatory bodies and/or the International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use [ICH] guidelines. Those guidelines set out the minimum data requirements for a new drug submission under long-term (12 months), intermediate (six months) and accelerated (six months) storage with varying temperature and humidity conditions. Throughout the assessment period the formulations are tested for assay values and impurity levels [see Chow Report #1, Exhibit 1].

[104] Dr. Chow's first report was based on stability data for three different formulation groups (A, B and C). Group A formulations (four formulations) had data covering at least eight weeks. Group B (nine formulations) had some four-week data. Group C (two formulations) had only the initial assay data.

[105] Dr. Chow reviewed Apotex's testing protocols and concluded they met ICH guidelines.

[106] Notwithstanding the preliminary nature of the data, Dr. Chow professed in his first report to be able to predict the stability outcomes for some of the formulations. According to Dr. Chow two of the Group A formulations "are expected to meet the acceptance criteria at the end of the stability program" for total impurities [see para 86]. For one of those formulations, he predicted a target shelf-life of two years. For the others, the data was insufficient to support a definitive two-year shelf-life.

[107] For four of the Group B formulations, Dr. Chow expressed the view that they "may well meet acceptance criteria at the end of the stability program and achieve a target shelf-life of two years" [see para 115(a)]. For the other four Group B formulations, Dr. Chow expressed uncertainty related to the interim impurity data obtained. The last Group B formulation failed to meet the required dissolution criteria.

[108] According to Dr. Chow both of the Group C formulations "meet the specification" [see para 124]. Because of the compositional similarities to Apo-Omeprazole, Dr. Chow expressed the view that Group C formulation MR8620E1 "would be expected to have sufficient stability since Apo-omeprazole is an approved product" [see para 125].

[109] Dr. Chow concluded his first report by stating that all of the NIA formulations would be readily scalable to commercial quantities.

[110] Dr. Chow updated his stability opinion in his report of January 6, 2017 by reviewing the stability data developed since his first report [Exhibit APO 131].

[111] For the two remaining Group A formulations, Dr. Chow dismissed an assay anomaly for one (despite not knowing the cause) and higher than expected impurity levels at 24 weeks under accelerated conditions for both. However, he did reduce his shelf-life expectation for both formulations to 18 months. He concluded that there was "a high probability that both formulations will meet acceptance criteria for at least an 18-month shelf-life" [see para 30].

[112] Of the Group B formulations, two were predicted to meet acceptance criteria for a two-year shelf-life [see para 47(a)], three had higher impurity levels and a predicted shelf-life of 18 months [see para 47(b)] and three did not meet specification criteria under accelerated conditions; nevertheless, one of those was predicted by Dr. Chow to have "a high probability" of an 18-month shelf-life while the other two were "less likely to meet specification criteria" [see para 47(c)].

[113] Dr. Chow reviewed the 16-week data for the Group C formulations. He dismissed an assay anomaly for one as being likely caused by poor sample preparation. He concluded that both were expected to continue to meet the requirements for drug release and "there is a high probability that both formulations will meet acceptance criteria for a 24-month shelf-life" [see para 60].

[114] AstraZeneca responded to Dr. Chow's opinions through Dr. Martin Davies. Dr. Davies had testified in the liability phase of this case and he was qualified to testify as an expert in physical chemistry, pharmaceutical stability, drug delivery and biomedical surface chemistry and in the development, testing and analysis and characterization of pharmaceutical formulations.

[115] Dr. Davies expressed the view that Dr. Chow's stability predictions were unsound because the supporting data were incomplete and, with one exception, the small-scale test batches were unsuitable to predict the stability of large scale commercially-produced products. Dr. Davies identified a number of problems in the scale-up of production that might be barriers

to success and he identified testing procedures that failed to meet the applicable stability guidelines. These included the failure to test more than one batch (to reduce the effect of batch variability) and the general failure to use pilot scale test batches (one-tenth commercial scale). Only one formulation met the pilot scale standard.

[116] Dr. Davies pointed out that Dr. Chow's first report was based on incomplete stability testing and, without completed testing, "there is insufficient data to reliably predict shelf-life" [Exhibit AZ 137, para 79]. He was particularly critical of Dr. Chow's extrapolation for Group C formulations for which only early data existed. He also criticized Dr. Chow for assuming linear degradation kinetics in the absence of empirical support and he challenged Dr. Chow's treatment of data anomalies.

[117] Dr. Chow's reply report addressed Dr. Davies' comments about the sufficiency of the incomplete stability data in the following way:

62. Many of the differences in the opinions of Dr. Davies and me appear to come down to the different perspectives from which we have looked at the stability studies conducted by Apotex. While I have looked at the stability studies to assess whether or not the formulations being studied would likely exhibit sufficient stability to be useful as a drug product, Dr. Davies appears to have focused on whether the studies, standing alone, could be presented to a regulatory agency, such as Health Canada, as part of a drug submission. I do not disagree with Dr. Davies that the Apotex studies in their present form would not be complete for filing with a regulatory authority as part of a drug submission. However, this does not mean that the studies fail to show whether the formulations are likely to have sufficient stability for use as a drug product. In general, by focusing on regulatory filings, Dr. Davies has failed to consider the realities of formulation development, and how stability studies are conducted and used in the pharmaceutical industry.

63. In light of Dr. Davies' opinions, it should also be understood that, as part of the formulation development process, formulations are initially prepared on a laboratory or pilot scale. Based on the test data obtained for these formulations, which will include abbreviated (as opposed to full-length) stability studies, formulators make informed predictions as to whether formulations are expected to possess the properties that are desired for the final dosage form. Scale-up of a formulation will only be conducted for formulations that are expected to be successful based on this initial testing of material prepared on a small-scale. For formulations that show sufficient stability in the lab or pilot scale, the formulator's expectation is that the formulation will also be stable when made on a larger scale using the same manufacturing steps.

64. Based on my experience in the pharmaceutical industry, I cannot recall an instance where the volume of information that has been collected for the Apotex formulations would not be considered to be suitable for deciding which formulation or formulations would be expected to be successfully scaled-up.

[Footnotes omitted.]

[118] Dr. Chow accordingly accepted Dr. Davies' point that the standards and methods employed by Apotex would not meet regulatory requirements. He said that, from a product development perspective, multiple batch testing was not required. He made the same point concerning the small lab tests batches. This, he said, was "a regulatory concern and does not relate to whether or not a formulation is stable, or expected to be stable" [see para 67].

[119] In response to Dr. Davies' criticism that Apotex's preliminary data were incomplete and insufficient to support a stability prediction, Dr. Chow stated, at para 73:

... At paragraph 60 of his Expert Report, Dr. Davies comments on the fact that, at the time of my September 6, 2016 Expert Report, the stability studies for the Group A, B and C formulations were not complete. As discussed above, this issue appears to be directed more to whether the studies could be submitted to a regulatory agency at that time, not whether the available information could be used to determine whether a formulation was likely to be stable throughout the duration of the stability program. However, as noted above (see paragraph 63), it is standard practice to use preliminary data from stability studies in order to determine which batch or batches to scale up.

...

74. In his Expert Report, Dr. Davies takes issue with my extrapolation of stability data, noting that the ICH Q1A stability guideline provides specific conditions for the extrapolation of stability. Again, Dr. Davies is confusing the regulatory guidelines for submitting stability data as part of a drug market application with the ability to predict whether a formulation is likely to be stable for the duration of a stability program. For a regulatory submission to Health Canada, Dr. Davies is correct that complete studies should be submitted, and that extrapolated data can only be relied upon in certain circumstances. However, I know from my own personal experience in the pharmaceutical industry that, during the development of a formulation, a portion of, or abbreviated, stability studies are routinely used to predict whether a given formulation is likely to have sufficient stability in long-term testing. During drug development, the time requirement to await the completion of a 6-month accelerated stability study is generally not available to a formulator, which makes predictions on less data a necessity to determine which formulations to progress.

[Footnotes omitted.]

[120] Dr. Davies' report dated March 23, 2017 took issue with Dr. Chow's updated stability opinions [see Exhibit AZ 138]. Dr. Davies maintained that the test data continued to be incomplete and the test methods continued to be deficient. He also noted that some of Dr. Chow's initial stability predictions proved, on further testing, to be unsound.

[121] Dr. Davies also noted a further testing anomaly in the form of progressive modifications to Apotex's assay methods which, over time, increased the assay results. These changes to sample agitation times indicated to Dr. Davies two potential problems: either the omeprazole in the samples was not, in the early testing, fully extracted or the formulations were undergoing physical changes making extraction more difficult over time (or a combination of both).

[122] Dr. Davies also drew attention to Dr. Chow's initial stability predictions for two of the Group B NIA formulations which, on further testing, proved to be unsound. He also pointed to decreased assay values and questionable impurity levels for several of the remaining formulations. He challenged Dr. Chow's 18-month shelf-life predictions for several of the formulations as speculation.

[123] In reply Dr. Chow agreed in theory with the need to validate assay testing methods but said in formulation development it is usually not done [see Transcript p 3107]. Full validation, he said, was required later in the process [Transcript p 3108]:

For example, you want to sell the product. It is a regulatory requirement to validate the method, so that you can sell the product -- make, test and sell the product.

Q. Surely you are validating for a reason beyond just regulatory requirements?

A. Certainly, because a product needs to be tested, and you want to have methods standardized, and you want to make sure that the method works.

He also accepted that assay testing methods should be kept constant "[a]s much as possible" although "[i]n development, we tend to revise methods from time to time" [Transcript p 3109].

[124] When questioned about Apotex's initial low assay values, Dr. Chow had "an idea about what could cause it" [Transcript p 3113] and was capable of designing an experiment to identify the exact cause [Transcript p 3114]. Nevertheless, he was not asked by Apotex to determine the cause.

[125] Dr. Chow also acknowledged the following points:

(a) he never calculated the degree of experimental error in the Apotex testing but he had an "idea" [Transcript p 3115];

(b) he was unable to measure batch-to-batch variations among NIA batches because only one batch of each was ever made [Transcript p 3116]. Single batch testing did not meet the regulatory standard [Transcript pp 3117-18];

(c) batch-to-batch variation will have an impact on shelf-life [Transcript pp 3118-19] and affects the degree of confidence "on production batches" [Transcript p 3119]. "[I]f you want to estimate shelf life accurately, you need multiple batches" [Transcript p 3122];

(d) when asked about his level of confidence in the absence of empirical data, he gave the following answers [Transcript p 3123]:

Q. When you are referring to "confidence," though, you are referring to it in a qualitative sense?

A. It is looking at the trend, yes. You can say that it is somewhat eyeballing and trending.

Q. So the answer to my question is "yes"?

A. Yes.

Q. You didn't quantify the confidence level of your predictions?

A. The term "quantify" means what?

Q. That you know the degree, the percentage of confidence in a statistical way?

A. From a statistical, 95 per cent confidence interval, I did not do it.

Q. You didn't do it for any confidence interval?

A. No.

(e) Dr. Chow made a “judgment call” about the linearity of degradation kinetics for the NIA formulations [Transcript pp 3185-3186];

(f) Dr. Chow admitted being “a bit optimistic” about some of his initial stability predictions [Transcript p 3192]. When challenged about his initial comparative assessment for two formulations that were similar, he gave the following answers [Transcript p 3193]:

Q. So your predictions based on linear degradation kinetics for all three of these formulations were incorrect?

A. Based on these three, yes, I was too optimistic. Those who fail continue to fail. Some of those that work still work. It is only one impurity I failed to address that, and that I can agree.

Q. In your opinion, experimental batch 151218A is expected to have similar stability to experimental batch 151215A?

A. I said in my report that it would have a similar stability profile and, also, in my report I -- responding report based on the 16-week data, accelerated condition, 218 is performing better than the 215.

Q. At the time of your first report, you were prepared to predict stability of 151218A based on 151215A?

A. Let me check my wording before I --

Q. Second sentence, paragraph 125, of your first report.

A. I state it would have similar stability.

Q. Now we know that 151215A no longer meets all the stability requirements?

A. It did not meet the stability requirement for one impurity, which is unknown impurity. It could be characterized later on.

Q. You are no longer using that batch to predict 151218A?

A. Well, I use that batch as a baseline, the 215A, for predicting 218A, because of the similarity in terms of composition.

Q. It turned out they don't have similar stability?

A. It is difficult to say what is "similar." One is slightly better than the other. Does this say "similar"? I will say it is still very similar. They all got the good side in terms of all studies -- all tests tested, except that the 218A is slightly better in terms of impurity.

Q. Well, 151215A is failing one of the specification requirements.

A. Yes, but if you look at the whole picture or the whole profile, both lots are performing very well, except for the one unknown impurity, and the unknown impurity level is still at a very low level. I agree that they are not making the acceptance criteria.

It does not necessarily mean that product is not useful as a pharmaceutical product. My mandate was to provide opinion whether it is a useful, potentially useful pharmaceutical product. I know that I may be more optimistic about stating the shelf life of that.

Passing the acceptance criteria that I would suggest, I would feel that it would likely make 24 months, but not making that unidentified impurity would not necessarily negate the point that it may still make a pharmaceutical product.

(g) all of the Group A formulations ultimately failed to meet one or more of Apotex's specification criteria [Transcript pp 3195-96];

(h) he agreed that an increase of 20 minutes in the sonification of test samples is a significant change to the assay test method and a 5% increase or more in assay results was a significant change [Transcript p 3259]. Without data the significance could not be determined quantitatively [Transcript p 3269]. A possible explanation for an increase in extraction time could be physical changes to the sample [Transcript p 3278];

(i) under Good Manufacturing Practice [GMP] protocols, the assay method cannot be changed [Transcript p 3281];

(j) different assay extraction methods required for Apo-Omeprazole and the NIA formulations "could" reflect the difference in behaviour [Transcript p 3282]; and

(k) Apotex did selective retesting of its NIA samples based on the "noticeably lower" assay results [Transcript p 3283]. This may not be an ideal approach but it is not uncommon for suspected samples [Transcript p 3285].

[126] Dr. Davies was cross-examined at length on his two reports. When asked about the propriety of overlooking an anomaly in accelerated stability data in favour of acceptable intermediate and long-term data, he gave the following responses [Transcript p 3538]:

Q. If you look at the guideline I have just given you -- let's try to expedite it. You accept it, too, provides that predictions can be made from intermediate conditions when there are significant changes in accelerated conditions?

A. I accept that when it is justified, when you can provide evidence through investigation why you would overlook the accelerated data and rely on the intermediate and long-term data.

[Emphasis added.] [See also Transcript p 3549.]

[127] Dr. Davies' concern was that Dr. Chow had provided no evidence to support such an approach with respect to the NIA formulations that presented in this way. Dr. Davies did accept that extrapolations of the sort made by Dr. Chow can be useful in the early stages of drug development and for selecting the best candidates [Transcript p 3546].

[128] Dr. Davies also challenged Dr. Chow's assumption that all of the NIA formulations had linear degradation kinetics. Dr. Davies observed that at least two of the formulations had non-linear degradation profiles [Transcript p 3568] and for others it was not possible to say without complete data [Transcript pp 3573-74]. He also pointed to prior art that showed omeprazole formulations "are prone to accelerated degradation" [Transcript p 3577].

[129] A significant issue of concern for Dr. Davies was the discovery that Apotex had made a series of changes to its testing protocols for the NIA samples.[1] Because of apparent problems in obtaining complete dissolution of those samples, Apotex substantially increased the agitation and sonification times from those employed in its earliest assays.

[130] In the face of those changes and in the absence of validation of the extraction method for the NIA formulations, Dr. Davies considered the data unreliable. The problem as Dr. Davies saw it was explained in the following exchange [Transcript p 3621-23]:

Q. With respect to the increased -- let's just first step back. The purpose of the assay is to accurately determine the amount of omeprazole in the pellets. Correct?

A. That would be the purpose of an assay. That would be what you would hope the assay would do.

Q. That is what Apotex was aiming to do in its study?

A. Sure. In the context of this, if you are changing your extraction method because you don't like the look of the results, if you are changing the assay method because you think the results are too low, that suggests a number of things. One, that the sample is changing, that it is becoming more difficult to extract. Or two, there is a problem with that extraction itself. That is just the least of them.

Q. Sample is changing or there is a problem with the extraction. I got you. Let's park that for a second and walk through this slowly with me, please. The purpose of an assay test is to -- that is the aim, to accurately determine the amount of omeprazole in the pellet?

A. I wouldn't disagree with that.

Q. That is to say you would agree with that?

A. That is the purpose in this case, is try to measure the amount of omeprazole that is present within the alternative -- the batch of the alternative formulations.

Q. You say that if you have failed to fully extract the omeprazole from the assay, then you are unable to reliably and accurately measure the omeprazole content?

A. I would agree with that.

Q. The purpose of the agitation in the assay is to try and get the omeprazole to properly dissolve within the dissolution media?

A. Properly dissolve in the solvent for extraction.

Q. Right. If it doesn't properly dissolve, you don't have all of the omeprazole. Therefore, you are not going to get an accurate result?

A. That is true. You don't know. That is true if you -- you don't know.

Q. Your objective in conducting an assay is to get the omeprazole dissolved so that you can ensure you have closer to the real result?

A. It is, but usually across -- if you are going to compare samples across time, you would use the same assay, a validated approach. You wouldn't need to change the assay over time. That is what begs the question: What if you use 90/60 on those initial results? What would we [sic] the value of those? We don't know. That is why you can't assume -- to your point -- that they have measured accurately in the initial results the value of omeprazole. We don't know.

[131] According to Dr. Davies, the increases in agitation and sonification times created the possibility that Apotex's earlier sample assays were under-reporting the levels of omeprazole. With that uncertainty it was not possible to do a valid comparison with later assays where optimum dissolution was obtained [Transcript p 3624].

[132] When it was then put to Dr. Davies that another possible explanation for the need for longer sample preparation time was that the samples were changing over time, he gave the following answers [Transcript p 3631]:

Q. The other possibility which you also raise is that you may have a problem with your assay. Correct?

A. It is possible.

Q. If the sample is changing over time, that doesn't mean you are actually losing omeprazole through the process, that you are not catching it. It means you have a sample that is changing over time that requires different agitation to get the omeprazole out?

A. They are not mutually exclusive. In the context of the sample changing over time, as a formulation scientist, you would be very concerned why that was occurring.

[See also Transcript pp 3632-36]

[133] The underlying problem with under-reported omeprazole assay values in the initial tests is that it has the potential to mask the amount of lost omeprazole as determined by subsequent assays. According to Dr. Davies this cannot be known from the extant data [Transcript p 3642]. This issue was more fully explained in the following exchange under direct examination [Transcript p 3398-3400]:

Q. Looking at the next set of comments you make, starting on paragraph 37, you say that:

"Apotex's investigations cast serious doubt on the reliability and accuracy of its assay method for measuring the omeprazole content of the alternate formulations." (As read.)

Could you explain why that is?

A. Yes, because these results revealed that extending the agitation times increases the assay results. We don't know the reason for that. It could be that the original assay time itself was insufficient to fully extract the omeprazole from the alternative formulations. Therefore, that calls into question all those initial results.

In a stability program, you are going to be comparing results against each other. The assumption is that you are analyzing each of them in the same way. But if your actual analytical method has been changed so it can increase the amount drug that is present, then that means you -- it makes it very difficult to compare results produced by different assay methods.

Q. Looking at your last set of comments on paragraph 39, you say that:

"Apotex's modifications to the assay method during the course of the stability program could have obscured 5 per cent or greater reductions in omeprazole content from the initial values." (As read.)

Could you explain how modifications could obscure such reductions?

A. Yes. The point I am making here is because you are not treating the initial results with the same analytical procedure, you are using less agitation than was used later in the testing, because we know 5 per cent or greater is a significant result.

If Apotex had tested those first set of data based on the information that we have, those results are likely to be higher. Therefore, failing to retest -- they can't retest because you can't go back. The very fact that they are retesting the later results could obscure a 5 per cent or greater reduction in omeprazole content. That is the point I am making.

JUSTICE BARNES: Just to clarify that, if you have an artificially low initial assay result and a true assay result later on, just clarify for me how that could obscure degradation or a "poor stability outcome," if I can put it that way.

THE WITNESS: I don't think we know what the true result later on is, Your Honour, because whether it is September or October or November, you are changing the assay as compared to the first result.

To say, for example, that you increase the results in September by 10 per cent, but you have done nothing to the initial results -- so say you have gone up from 90 per cent to 100 per cent in September. It was originally 90 per cent but you have increased it by 10 per cent. The value at the beginning could be, say, 95 per cent.

Well, you could increase -- if you use the same agitation time for the initial results, based on the data here, it seems to indicate you have better extraction, so that 95 result may become 105 result per cent. So now instead of having 95 and 100 per cent -- 95 for the initial and 100 per cent for the retested sample in October or September -- you now have the retested initial result, 105 per cent, compared to 100 per cent. So you now have, potentially, a 5 per cent or more change, but Your Honour will never know.

Because if you are changing -- if you are trying to compare results all the way through when your analytical method is changing because you recognize you are not extracting all the omeprazole, what about the results at the beginning, which is your baseline, where you start from? That is what makes it difficult.

[134] The fundamental difference between Dr. Chow and Dr. Davies concerns the scientific weight that should be attributed to the stability data produced by Apotex's in-house testing. On this issue, I prefer the evidence of Dr. Davies to that of Dr. Chow.

[135] Dr. Chow was forced to make predictions based on incomplete data. The initial predictions he made were based on very early data and, not surprisingly, some were later shown to be unsound. But Dr. Chow's apparent willingness to rely on preliminary and inconclusive data says something about his credibility – albeit within the context of an early stage drug development scenario.

[136] Like Dr. González's use of IVIVR to predict bioequivalency, Dr. Chow approached the problem of NIA stability as though it was a formulation screening exercise. Although Dr. Chow acknowledged some of the issues raised by Dr. Davies as having potential relevance to the process for achieving regulatory approval, he felt that, for his more limited purposes, the methods he employed and the data he reviewed were sufficient to make some reliable predictions about the stability of the tested NIAs. My reservations about this approach as they applied to Dr. González's opinions apply equally to Dr. Chow's predictions. Early and incomplete data are just that. They do not support an inference of regulatory and commercial viability simply because a formulator might find them useful for internal screening purposes.

[137] Dr. Davies approached the test data from a far more rigorous perspective – a perspective that was generally in keeping with the standards that would be required to commercialize the asserted NIAs. This was the better approach because it was commensurate with the ultimate burden of proof.

[138] Apotex has attempted to justify its stability testing shortcuts and incomplete test data largely on the strength of its claimed entitlement to a standard of proof that is lower than the applicable regulatory requirements. In short, it says the Court should draw an inference that at least some of its NIA formulations would have been more likely than not to be sufficiently stable to obtain regulatory approval and commercial success.

[139] On the evidence presented, I am not prepared to draw that inference.

[140] Although Dr. Chow's stability analysis rests, in part, on empirical data, the results were incomplete.

[141] To the extent that Dr. Chow attempted to minimize the shortcomings of Apotex's stability testing methods and the significance of the observed data anomalies noted by Dr. Davies, I reject Dr. Chow's views. The concerns raised by Dr. Davies about batch variability, batch size and the lack of validation were valid and cast doubt on the reliability of the obtained test data.

[142] The numerous changes Apotex made to its NIA sample preparation and its selective retesting also undermine the value of the initial assay data. I accept Dr. Davies' point that it is not possible to fully understand the significance of those changes, but it was Apotex's burden to complete its stability testing in a way that would eliminate this type of avoidable uncertainty. It seems inescapable to me that where the baseline assay data are suspect, downstream extrapolations from those data are also rendered suspect. Apotex's attempts to rehabilitate those data by reference to the observed impurity and mass balance data were insufficient and unconvincing.

[143] Dr. Davies is correct that Apotex's methodological changes and selective retesting introduced an unacceptable degree of error to the process. The initial assay values were rendered almost worthless for comparison purposes – at least far from a level of certainty required for my purposes. I accept Dr. Chow's point (concurred in by Dr. Davies) that shortcuts like the ones employed by Apotex may be acceptable in the early stages of product selection, but they are entirely unacceptable in the context of proving the viability of a NIA for the purpose of this case.

B. Would the Proposed NIAs Have Received Regulatory Approval? [144] Apotex contends that, for regulatory purposes, it could have piggy-backed its NIAs on the approval it received for Apo-Omeprazole. Under this hypothesis, once Apo-Omeprazole obtained regulatory approval, it would be a routine and simple exercise to obtain an approval for each of the NIAs. According to this argument, Health Canada would have accepted any of the seven now-asserted NIAs as minor variants to Apo-Omeprazole such that robust bioequivalency testing would not have been

required for approval. This idea is, of course, wholly belied by what Apotex actually did in the face of its knowledge that Apo-Omeprazole was likely an infringing product and it is inconsistent with what the regulators would have accepted. Indeed, the theory is based on an apparent assumption that the regulators would not have followed applicable guidances nor applied robust due diligence to the approval of the submitted NIAs.

[145] Each of the parties led evidence from a qualified witness with expertise in Canadian regulatory affairs. Apotex called Ms. Sue Wehner and AstraZeneca called Ms. Anne Tomalin. The fundamental differences between these witnesses concerned the likely willingness of Health Canada to deviate from its own guidances and whether bioequivalency testing would have been required for Apotex's seven remaining hypothetical NIAs.

[146] Where they differ, I prefer the evidence of Ms. Tomalin over the evidence of Ms. Wehner. I do not accept that all of the NIAs involved minor changes to the formulation for Apo-Omeprazole and that, with the exception of Formulation MR8620E1, Health Canada would have accepted notifiable change requests [NCs] for the proposed NIAs.

[147] Ms. Wehner's analysis depended largely on her characterization of Apo-Omeprazole as an immediate release drug, as opposed to modified release, and on her reliance on Dr. González's unsound bioequivalency data. Ms. Tomalin described Ms. Wehner's approach as follows [Transcript p 3841]:

As I understand what Ms. Wehner did, she started with her understanding of omeprazole and that omeprazole, in her view, was an uncomplicated product. She looked at the data supporting the changes and felt that the data confirmed that the changes being made were not significant changes, and from there, went to a conclusion that the type of submission that would be required would be a notifiable change.

[148] In contrast, Ms. Tomalin's analysis depended on Health Canada's published policies and guidance documents at the relevant time. While they may not technically have the force of law, the real question is whether they were used by Health Canada at the relevant time to interpret the applicable statutory and regulatory requirements. I accept Ms. Tomalin's evidence that Health Canada did strictly follow its guidance documents over the relevant period.

[149] I also accept Ms. Tomalin's evidence that Apo-Omeprazole is a modified release product, as that term is understood by Health Canada. There is ample support for this conclusion in the guidance documents. For example, the 1996 Bioavailability and Bioequivalence Studies document clearly defines a modified release product as including formulations designed to delay absorption, such as enteric-coated forms [see Exhibit E-2 to Wehner Report #1, Exhibit APO 50, p 2]. This approach was confirmed in the later Post-NOC Changes document which defined modified release solid oral dosage forms as including "both delayed and extended release drug products" [see Exhibit E-5 to Wehner Report #1, p 229].

[150] I do not accept Ms. Wehner's evidence that a qualitative change to either an excipient or to an enteric coating would be treated by Health Canada as insignificant. The better evidence came from Mr. Len Arsenault based on his experience working at Health Canada where he was manager of the oral products division of the Bureau of Pharmaceutical Sciences. Mr. Arsenault – now vice president of scientific affairs with Sandoz - was called by Apotex to speak to the history of Sandoz's omeprazole product. He testified that Health Canada considered an enteric coated formulation to be a modified release product for which an alteration typically required the submission of bioequivalency data [Transcript pp 1735]. Like Ms. Tomalin, he also testified that the switch from one kind of polymer to a different enteric coating polymer or a qualitative change to an excipient would require proof of bioequivalency [see Transcript pp 1742, 1744-45].

[151] I also do not accept Ms. Wehner's evidence that a change in the solvent used in the coating process, from water to organic solvents, would not be considered a significant change. Ms. Wehner's conclusion is inconsistent with a 1997 letter from Health Canada advising that "[i]n the case of delayed-release or other modified-release preparations whose coatings affect drug release," a supplement is required when a change is made to the tablet coating [see Schedule D-5 to Tomalin Report #1, Exhibit AZ 155, p 3]. I prefer Ms. Tomalin's evidence that these requirements would apply because the enteric coating of Apo-Omeprazole affects drug release by delaying the release of omeprazole until it reaches the small intestine. I also accept that this document would be applied equally to both tablets and pellets.

[152] Finally, I do not accept Ms. Wehner's conclusion that changes from wet to dry granulation would not likely be considered significant. This conclusion was based primarily on Ms. Wehner's opinion that Apo-Omeprazole was considered to be an immediate release drug with rapid dissolution, which I do not accept. I prefer the evidence of Ms. Tomlin who stated that Health Canada would have viewed the change as one requiring supporting bioequivalence data and the submission of a supplement because it is a change that could have an impact on bioequivalence. This was eventually expressly reflected in the 2007 guidance, which Ms. Wehner acknowledged [see Transcript p 1561].

C. Would Apotex Have Obtained and Used a Third-Party NIA? [153] Dr. Sherman testified that he could and would have obtained a NIA from a third-party source, but only if he was unable to develop an in-house formulation. From this evidence I can only conclude that if a third-party option was required, it would only have been pursued after Apotex had tried and failed to produce and commercialize its own formulation. At best this option would only have been pursued well into the infringing period and would have required Canadian regulatory approval.

[154] I do accept that, in theory, there were NIAs potentially available to Apotex from two sources. Those sources were Kremers Urban Development Company [Kudco] and Estevé.

[155] Evidence concerning the Estevé omeprazole formulation was given by Ms. Cinta Lacasa Pujadó. Ms. Lacasa holds a senior management position with Estevé and is responsible for regulatory affairs, intellectual property, pharmacokinetics and product development.

[156] Estevé is a Spanish-based pharmaceutical company. It produces both innovative and generic products and has business relationships with both Apotex and AstraZeneca.

[157] According to Ms. Lacasa, Estevé began to develop an omeprazole formulation in the late 1980s. By 1994 or 1995 it had a marketable and patented omeprazole formulation. At that time Estevé's business model was limited to the sale of its own innovative drugs. It was not equipped to sell generic formulations and, thus, it supplied its omeprazole formulation only to interested third parties. In the United States Estevé entered into a contractual relationship to supply its omeprazole product in pellet form to Mylan. Mylan encapsulated the pellets for sale into the United States. Mylan was also responsible for obtaining regulatory approval in the United States, albeit with technical support coming from Estevé. It was not until mid-2003 that Mylan obtained United States regulatory approval.

[158] After Mylan launched the product in the United States in August 2003, Mylan and Estevé were sued for infringement. That suit was successfully defended on the basis that the Estevé pellets did not infringe AstraZeneca's United States patent. After obtaining Canadian regulatory approval, Mylan began to sell the same omeprazole formulation in Canada in 2009. Estevé assisted Mylan with its Canadian regulatory filings in 2007 and later.

[159] When Ms. Lacasa was asked about Estevé's hypothetical interest in supplying its omeprazole formulation to Apotex, she said it would have been "[v]ery much interested" and would have provided the necessary technical support for a Canadian regulatory submission [see Transcript p 2940].

[160] Ms. Lacasa went on to say that Estevé would have needed Mylan's approval to sell its omeprazole product to Apotex. Mylan's agreement was required because the governing contract with Estevé gave Mylan exclusive distribution rights in the United States, Canada and Mexico.

[161] Before Mylan entered the market, neither Apotex nor any other party had approached Estevé about supplying the Canadian market. However, in the case of Mexico, Estevé was approached by a third party in 2003 or 2004 to supply its omeprazole product and Mylan unconditionally waived its exclusivity rights in that country.

[162] According to Ms. Lacasa, Estevé had more than ample production capacity to fully meet Apotex's supply requirements. Its usual terms of sale for similar third-party sales of its omeprazole were in the range of 25 to 35% of net sales depending on the specific details of each case [see Transcript p 2953].

[163] Over an objection from AstraZeneca's counsel, I allowed Ms. Lacasa to speak to the issue of Mylan's likely willingness to waive its Canadian rights. She answered that Mylan had done so in Mexico and, at the same time, it had no commercial presence in Canada. She concluded with the statement: "[t]here could have been additional business also for Mylan, depending on the type of arrangement that we could have created" [Transcript p 2956]. Later she said "[e]veryone needs to gain something" [Transcript p 2994].

[164] Under cross-examination, Ms. Lacasa confirmed that Estevé's development of a non-infringing omeprazole formulation for supply to Mylan took from 1995 to the point of filing a United States ANDS in 2000. It was only in 2003 that the product was actually launched into the United States. During the five years of product development, a number of formulations were tested involving "a lot of work" [Transcript p 2973]. Ms. Lacasa also acknowledged that "[o]meprazole has been a very difficult product" and a number of its bioequivalence studies failed [Transcript p 2975].

[165] It is of some significance that, when Ms. Lacasa was asked if Mylan would have permitted Estevé to supply its omeprazole formulation to Apotex for sale into the United States, she observed that those companies competed in that market. She concluded with the statement that "[t]his is something we should ask Mylan. I don't know" [Transcript p 2990].

[166] Based on Ms. Lacasa's testimony, I am satisfied that Estevé had the manufacturing capacity to supply its non-infringing formulation to Apotex in sufficient quantities to substitute for Apotex's sales of Apo-Omeprazole.

[167] I do not, however, accept that the evidence before me is sufficient to establish that Apotex would have been able to obtain a supply agreement from Estevé.

[168] It is very apparent that Mylan would never have allowed Apotex entry to the United States market with Estevé's product. Mylan had invested heavily in the further development and approval of Estevé's omeprazole formulation for sales into the United States market. According to Ms. Lacasa, Mylan had captured a significant portion of that generic market with that formulation. In those circumstances, it is inconceivable that Mylan would have waived its exclusive rights in favour of a generic competitor.

[169] Notwithstanding Mylan's North America rights, it did allow Estevé to sell the formulation to a third party in Mexico. Mylan had no commercial presence in Mexico and one can presume it was commercially indifferent to that market. I do not agree, though, that this experience can be extended to the Canadian market in the hypothetical world. In the real world Mylan did enter the Canadian market with the Estevé formulation in 2009 and Estevé assisted with that process beginning in 2007. Presumably, Mylan began to contemplate an entry to the Canadian market even earlier than 2007. The likelihood that Mylan would have waived its Canadian rights in favour of a significant competitor seems very remote. As Ms. Lacasa noted, businesses are not in the business of doing significant favours for their competitors. Rather, they exploit their commercial advantages.

[170] In order to establish the conditions under which Mylan may have considered a waiver of its exclusive distribution rights, Apotex should have called a Mylan witness. In the absence of that evidence, I am not persuaded that Apotex could and would have obtained a NIA from Estevé.

[171] Given the evidence of Dr. Sherman, I also doubt that Apotex would have come to terms with either Mylan or Estevé under some form of licensing agreement, even if the opportunity presented itself.

[172] Apotex also led evidence about the hypothetical availability of a non-infringing omeprazole formulation to be supplied by Kudco. Kudco is the United States subsidiary of the German pharmaceutical company Schwartz Pharma and it held the United States rights to a non-infringing omeprazole formulation under license from a French company, Pharma Pass. Kudco sought regulatory approval in the United States for its capsule product in mid-1998 by way of an ANDS. It received a conditional approval in 2001 subject to the resolution of outstanding infringement proceedings with AstraZeneca. Final regulatory approval was granted in 2002 when the Kudco product was found to be non-infringing. Until August 2003, Kudco was the only generic entrant in the United States market.

[173] Kudco's Chief Financial Officer at the relevant time was Jon Thiel. Mr. Thiel was called on behalf of Apotex.

[174] Mr. Thiel testified that in the period of 2001 to 2003 Kudco did not have a business presence in Canada and did not supply its omeprazole product to the Canadian market. Nevertheless, he was asked if Kudco would have, at the time, been interested in entering into a business relationship with Apotex for sales into Canada. In response, he gave the following testimony [Transcript p 1615]:

A. We were a company that tried to be very opportunistic in terms of creating additional revenue sources. Canada was, as I stated, not a market that we were in. With the proper capacity and obviously the proper financial terms, it would have been attractive to us.

It was an easy way to get into Canada. Assuming that Apotex would have done the regulatory stuff within Canada, it would have been an easy way for us to get in the market and gain additional profits.

Q. Would Kremers have had to have sought permission from Schwarz or anyone to enter into such an arrangement?

A. When you say "Schwarz"?

Q. Schwarz Pharma.

A. U.S., Germany? There are quite a few of us.

Q. Let's say the German operation.

A. For something like this, no.

Q. Was that a decision that would have been made locally within your group at Kremers KUDCo?

A. Yes, the small team that ran the brand and generic in the U.S. would have made that decision.

Q. You were a part of that team?

A. Yes, I was.

Q. Would the omeprazole product have been any different from the product that was sold in the United States?

A. No, it would not have been.

Q. Would Kremers or KUDCo have had the capacity to supply Apotex with omeprazole capsules?

A. Over time, yes. As soon as we launched, we started increasing capacity daily. We made significant investments in our Seymour facility, both in terms of machinery and equipment, people, increased shifts.

So as soon as we had approval from the FDA to launch, I think immediately we knew that if we increased capacity, it would pay off -- I don't remember anymore. It was days. We substantially increased capacity every day.

Q. You mentioned that you took some steps. What year did you take those steps in?

A. As soon as we got approval, so that would -- I would have to -- I don't recall at the time of launch, anymore, what our capacity was. But as soon as we got into November of 2002 when we knew we were alone in the market, that is when we started increasing capacity over and above what we already had.

[175] AstraZeneca objected to this line of questioning on the basis that it called for an inadmissible lay opinion. I allowed the evidence provisionally.

[176] I take AstraZeneca's point that there are clear dangers with asking a witness directly about what he or, more to the point, his employer would have done in the context of a hypothetical environment. Questions about the extant factual conditions that would have been relevant to the decision are appropriate. Answering the bare question of "what would you have done" carries very little, if any, weight. In this case the answers provided by Mr. Thiel are factually relevant and admissible.

[177] Mr. Thiel was asked about the terms that Kudco would have required to do business with Apotex. This line of enquiry is appropriate insofar as it has a factual foundation rooted in the business terms that typically applied to similar arrangements. Mr. Thiel was also the appropriate witness to speak to this issue because he was the manager who was, at the time, involved in these types of negotiations. His answers are instructive of the terms that Kudco would likely have sought and accepted, at least with respect to sales into the Canadian market [Transcript p 1617]:

Q. Mr. Thiel, let's assume for a moment that Apotex and Kremers or KUDCo decided to enter into a supply agreement. How would Kremers have priced its capsules for purchase by Apotex?

A. What we typically did is we charged our customers our cost of goods.

Q. Would there be any additional remuneration that would be required in addition to your cost of goods?

A. Yes. We would have required some type of a profit share, gross profit share, usually anywhere from 25 to upwards -- we go as high as we could, quite honestly. We would try to get 50 per cent if we could.

Q. All right, so somewhere in that range. Where do you think you ultimately would have ended up?

A. It is hard to say, obviously, because we are kind of in the hypothetical world. Obviously, we would have asked for 50 and they would have said, "How about five or 10" or whatever. And 30 or 40 per cent, I would guess.

Q. Can you tell me, is that similar to the range that other agreements were entered into with other companies?

A. I don't specifically recall "yes." Again, having done this now, obviously with Schwarz as well as County Line, my experience as a pharmaceutical finance person, yes, that is kind of the range -- is 25 to 50 per cent these days.

Q. Assuming that financial terms were agreed upon, do you believe it likely that such an agreement would have been entered into with Apotex?

A. Yes.

Q. We have been talking about Canadian sales. Would Kremers have been willing to do a deal for sale of an Apotex product into the United States after competition you had already gone and received generic competition in the U.S. market?

A. Would we have considered it? Was that your question?

Q. Yes.

A. Yes, I believe we would have. Again, as I said, we were very opportunistic. We were a relatively small pharmaceutical company for the U.S. standards and we were very aggressive as -- I guess "aggressive" is the right word -- as it came to creating profit opportunities.

Certainly if the conditions were right in terms of if there was so much competition, we understood that at some point, to make money, more volume helps. When you own a manufacturing facility, you bring your costs down by running more volume through it.

It is free money, at some point. So yes, we absolutely would have considered it, again, with the right conditions in terms of competition and everything else to run -- to sell to a competitor, yes.

Q. That includes a competitor even in the same jurisdiction where were you [sic] operating?

A. Yes.

[178] Under cross-examination Mr. Thiel confirmed that between 2001 and 2008, Apotex made no enquiries about obtaining the Kudco formulation. During the same period, Kudco neither sold its formulation to any other generic company nor did it approach another company with a view to doing business.

[179] Mr. Thiel was unable to recall if Kudco had the legal right to sell its omeprazole formulation to Apotex under the terms of its assignment agreement with Pharma Pass and that agreement was not put into evidence.

[180] Mr. Thiel also acknowledged that he was being paid $500 (USD) per hour for his preparation and trial testimony.

[181] Further evidence concerning the hypothetical availability of the Kudco omeprazole formulation was provided by Mr. Tom Lewis. Mr. Lewis started working as Kudco's Plant Controller in 1999. In that role he was responsible for the financial activities of the business and strategic and capacity analysis. He reported to Mr. Thiel.

[182] Mr. Lewis testified that under the terms of the licensing agreement with Pharma Pass and, with the exception of Europe, there were no restrictions on Kudco's right to sell its omeprazole formulation to a third-party.

[183] According to Mr. Lewis, the licensing agreement could not be produced because of business confidentiality concerns. Nevertheless, he professed to be intimately aware of its terms.

[184] Mr. Lewis described Kudco's manufacturing capacities in considerable detail in terms of producing its omeprazole formulation, including the efforts it made to increase capacity in response to demand. He summed up that evidence in the following way [Transcript p 1670]:

Q. Let me ask you that question again. If, in the period 2001 to 2003, Apotex approached Kremers and asked whether it would have been interested in entering into a supply agreement for the sale of Kremers' omeprazole product in Canada, would this have been something Kremers would have been capable of doing?

A. Yes.

Q. Why do you say that?

A. At that same time, there were multiple other third parties that were approaching us to do additional production for them in our facility, and we accepted the majority of those and started manufacturing for those companies.

Q. I want to ask you specifically if Apotex had needed one million 20 milligram capsules in 2003, 26 million capsules in 2004, 63 million capsules in 2005, 115 million capsules in 2006, 150 million capsules in 2007, and 133 million capsules in 2008, are any of those numbers I have given you on a yearly basis beyond the capability or within the constraints of Kremers?

A. We would have easily been able to do that.

Q. Would a supply deal with Apotex have been something Kremers would have been willing to consider?

A. We would have.

Q. Why do you say that?

A. As I mentioned earlier, we had multiple third-party companies that were approaching us to do business for them, to manufacture for them, and we were doing that because we had excess capacity to lend to them.

[185] Under cross-examination Mr. Lewis was asked what Kudco typically expected as a royalty under its third-party supply contracts. Like Mr. Thiel he said the negotiated rate could be as high as 50% but “probably 20 to 50 percent, maybe 30 to 50 percent” [Transcript p 1692]. He also confirmed that Kudco did not historically supply its products to other generic competitors for the United States market [Transcript p 1696].

[186] Dr. Sherman also gave evidence about what Apotex would have done to obtain a NIA formulation from either Estevé/Mylan or Kudco and on what terms. When asked about his willingness to pay a royalty rate as high as 50%, he used the word “exorbitant” [Transcript p 1959]. In direct examination he went on to describe a likely hypothetical negotiation in the following terms [Transcript p 1960]:

Q. Let's say they insisted on cost plus a profit share, what would your reaction be?

A. I would say fine if it is going to be cost plus profit instead of markup, it should be your net cost plus some modest percentage of the profit.

Q. What if they had insisted on 40 or 50 percent?

A. If they had insisted and I had no option, I would have to take it I suppose, but that is unlikely because they wouldn't know that I would have no option. It is first of all not likely to happen, but secondly, they wouldn't know I had no other option. It is most unlikely.

If it were, in fact, the case I had no option and they knew I had no option, then I would accept it. It is not likely that would end up that way. It is more likely they would say, "Fine. Let's do it at cost plus 20 percent or a 10 percent royalty or some compromise." That would be the most likely outcome.

[187] Under cross-examination, Dr. Sherman conceded that no attempt was ever made to obtain a non-infringing third-party omeprazole formulation or to reflect on the terms of any such arrangement [Transcript p 2192]:

Q. During the life of the 693 Patent, Apotex never asked Mylan, KUDCo, or Lek to supply omeprazole product to Apotex?

A. No. Of course not. There was no reason to do so. If there had been reason to do so, I would have.

Q. During the life of the 693 Patent, Apotex never knew what it would cost for anyone to supply it with an omeprazole product using the KUDCo, Lek, or Mylan processes?

A. I would have to discuss it with them and negotiate to find out.

Q. The answer would be you didn't know?

A. Of course not. I could have guessed.

Q. Am I correct that Apotex never sought or obtained a license from anyone to make, use, or sell any omeprazole formulations using the KUDCo, Mylan, or Lek process during the life of the 693 Patent?

A. Sorry. You are contemplating I would make it using their process when I didn't know the details?

Q. You never sought or obtained a license from anyone to make, use, or sell any omeprazole formulations using the KUDCo, Lek, or Mylan processes?

A. Of course not. I wouldn't need a license. If I wanted to make a product without an ARC, I wouldn't need a license. I could do it far better and design a formulation in a matter of minutes that is better than that used by any of the three of them according to what is in their patent.

[188] Dr. Sherman's explanation for this was given in the following way [Transcript p 2115]:

Q. Let me explore that. You were sued in the United States?

A. Yes.

Q. In 2000, thereabouts, when the action started in the U.S.?

A. Yes, 2000-2001. I am not sure.

Q. You never took any steps to mitigate or to investigate the existence of a subcoating in your products?

A. Now you are getting back to the same issue, the one about semantics. We are going to have this with every question unless I can give you my understanding now.

Q. You never took any steps to develop a non-infringing alternative after you were sued in the United States; correct, until 2001?

A. We had a non-infringing product, and I couldn't predict the basis upon which a court would find otherwise.

Q. You never took any steps after you lost, in the United States litigation in 2007, to switch to a non-infringing alternative. Correct?

A. Again, there is a premise in there that the product was infringing. It was found to be infringing in the United States. That doesn't mean that it was in fact infringing, nor it would be held infringing in Canada.

[189] The above evidence establishes that there was some potential for Apotex to license the Kudco NIA on some basis at some point. Mr. Thiel and Mr. Lewis testified that Kudco was opportunistic and would likely have sought a royalty of 50% of the gross profits earned from Apotex's Canadian sales and might have settled for something in the range of 30% to 40%. Kudco also had no direct means to access the Canadian market and it had excess manufacturing capacity.

[190] A major problem for Apotex, though, is that no deal would have been available to it until Kudco had established that its omeprazole formulation was non-infringing. That finding was made by the District Court in late 2002 and affirmed on appeal a year later. It was only in this time-frame that Apotex could have realistically sought regulatory approval from Health Canada for the Kudco product. It is also noteworthy that the Kudco product had been approved in the United States with Prilosec (AstraZeneca's omeprazole product for sales into the United States) and not LOSEC (the Canadian product) as the reference product. This is significant because when Apotex sought approval for Apo-Omeprazole one of the major hurdles it faced in Canada involved its use of Prilosec as the reference product. Furthermore, given Dr. Sherman's evidence that Apotex would only have considered a third-party source if its in-house approach failed, I do not think this NIA strategy could have been realistically pursued until well into the infringing period.

[191] An even larger problem with this theory is the weakness of the evidence tendered by Apotex concerning the commercial terms that could have been expected in reaching a licensing agreement with Kudco. I do not accept that reaching such an agreement would have been as routine as Dr. Sherman suggested. Dr. Sherman expected to do a deal for a "modest" royalty in a likely range of 10 to 20%. In the United States District Court proceeding, Apotex took the position that a license fee of no more than 7% was warranted [see AstraZeneca AB v Apotex Corp, 985 F Supp 2d 452 (2013)]. Kudco on the other hand typically negotiated a higher rate of return of 30 to 40%.

[192] This kind of evidence is not very helpful. Evidence in the form of an economic model would have been more persuasive than this kind of hypothetical anecdotalism. I am not, therefore, satisfied that Apotex is more likely than not to have entered into some form of licensing agreement with Kudco during the infringing period. If I am wrong about the standard of proof that applies such that the test in Athey v Leonati, [1996] 3 SCR 458, 140 DLR (4th) 235, is applicable, I would fix the possibility of reaching an agreement with Kudco to supply the Canadian market by the beginning of the infringing period at 15% and at a royalty rate of 35% on Apotex's net sales.

[193] I also do not accept the evidence of the Kudco witnesses insofar as they suggested Kudco would have considered licensing Apotex to sell into the United States market. I think it is highly unlikely that Kudco, as a leader in the generic market for omeprazole, would have seriously considered an arrangement to further divide the United States market – at least on terms Apotex would have entertained. The evidence from Mr. Thiel and Mr. Lewis about the contractual basis for allowing entry to Apotex was simply too vague to support such a finding. Indeed, this is an inherent weakness in promoting a NIA theory on the strength of assumptions that have little or no historical precedent.

[194] I would add one more concern about the evidence of Mr. Thiel. He acknowledged under cross-examination that he was receiving $500 (USD) per hour from Apotex for time spent in preparation and in giving his trial testimony. The practice of paying fact witnesses substantial sums to testify about the likelihood of hypothetical events is suspect, at least when it goes beyond an indemnity for lost income. The hindsight nature of the enquiry coupled with the incentive to provide an answer the payor is looking for – or to colour the answer on favourable terms – makes the practice particularly questionable. To the extent Mr. Thiel expressed an optimistic view of the hypothetical prospects of doing business with Apotex, I discount that evidence.

D. Conclusion on the Availability of a NIA [195] Dr. Sherman's testimony that it would have been a simple, straight-forward exercise to develop a commercially viable NIA to Apo-Omeprazole is belied by history. That was not Apotex's experience with Apo-Omeprazole and it was not Estevé's experience with its non-infringing formulation. That was also not Apotex's experience with the numerous NIA formulations it tried, most of which, by its own acknowledgement, failed. In the end, Apotex has asserted seven alternative formulations but, as noted above, not one of them has been shown to be approvable and commercially viable. For the reasons given above, I also do not accept that Apotex would have obtained a NIA from a third party.

[196] Apotex has, therefore, failed to prove on a balance of probabilities that it would have had an available NIA omeprazole formulation at any time during the infringing period in any of its markets.

III. How Should the Court Reconcile the Section 8 Judgment in Favour of Apotex in Court Docket T-2300-05 with the Infringement Judgment in Favour of AstraZeneca in Court Dockets T-1409-04 and T-1890-11 [197] The parties have agreed on the quantum of Apotex's claim in the section 8 reference. The only questions left for my determination are whether Apotex is entitled to recover that amount having regard to a) its corresponding infringement of the 693 Patent and to b) its NIA defence to recovery by AstraZeneca for that infringement. As discussed above, I have found that Apotex did not and would not have had an available NIA during the infringing period. The only remaining issue concerns the interplay between the section 8 Judgment favouring Apotex in Court file T-2300-05 and my Judgment finding for AstraZeneca in Court files T-1409-04 and T-1890-11.

[198] According to Apotex its entitlement to damages is fixed and final and cannot be redetermined. Apotex relies on a series of judgments rendered in its favour by this Court and by the Federal Court of Appeal which, based on principles of res judicata and abuse of process, it contends prevent the issue of its section 8 entitlement from being relitigated.

[199] AstraZeneca has a different view of the significance of the earlier litigation history and says it is not estopped from making a case for a nil recovery by Apotex. According to AstraZeneca's argument, Apotex has not suffered any financial loss but only a lost opportunity to unlawfully infringe the 693 Patent.

[200] As a starting point to this part of the analysis it is important to consider some of the underlying principles to a claim to section 8 damages. Section 8 of the Patented Medicines (Notice of Compliance) Regulations, SOR/93-133 [NOC Regulations] provides:

8 (1) If an application made under subsection 6(1) is withdrawn or discontinued by the first person or is dismissed by the court hearing the application or if an order preventing the Minister from issuing a notice of compliance, made pursuant to that subsection, is reversed on appeal, the first person is liable to the second person for any loss suffered during the period

8 (1) Si la demande présentée aux termes du paragraphe 6(1) est retirée ou fait l'objet d'un désistement par la première personne ou est rejetée par le tribunal qui en est saisi, ou si l'ordonnance interdisant au ministre de délivrer un avis de conformité, rendue aux termes de ce paragraphe, est annulée lors d'un appel, la première personne est responsable envers la seconde personne de toute perte subie au cours de la période :

(a) beginning on the date, as certified by the Minister, on which a notice of compliance would have been issued in the absence of these Regulations, unless the court concludes that

a) débutant à la date, attestée par le ministre, à laquelle un avis de conformité aurait été délivré en l'absence du présent règlement, sauf si le tribunal conclut :

(i) the certified date was, by the operation of An Act to amend the Patent Act and the Food and Drugs Act (The Jean Chrétien Pledge to Africa), chapter 23 of the Statutes of Canada, 2004, earlier than it would otherwise have been and therefore a date later than the certified date is more appropriate, or

(i) soit que la date attestée est devancée en raison de l'application de la Loi modifiant la Loi sur les brevets et la Loi sur les aliments et drogues (engagement de Jean Chrétien envers l'Afrique), chapitre 23 des Lois du Canada (2004), et qu'en conséquence une date postérieure à celle-ci est plus appropriée,

(ii) a date other than the certified date is more appropriate; and

(ii) soit qu'une date autre que la date attestée est plus appropriée;

(b) ending on the date of the withdrawal, the discontinuance, the dismissal or the reversal.

b) se terminant à la date du retrait, du désistement ou du rejet de la demande ou de l'annulation de l'ordonnance.

(2) A second person may, by action against a first person, apply to the court for an order requiring the first person to compensate the second person for the loss referred to in subsection (1).

(2) La seconde personne peut, par voie d'action contre la première personne, demander au tribunal de rendre une ordonnance enjoignant à cette dernière de lui verser une indemnité pour la perte visée au paragraphe (1).

(3) The court may make an order under this section without regard to whether the first person has commenced an action for the infringement of a patent that is the subject matter of the application.

(3) Le tribunal peut rendre une ordonnance aux termes du présent article sans tenir compte du fait que la première personne a institué ou non une action en contrefaçon du brevet visé par la demande.

(4) If a court orders a first person to compensate a second person under subsection (1), the court may, in respect of any loss referred to in that subsection, make any order for relief by way of damages that the circumstances require.

(4) Lorsque le tribunal enjoint à la première personne de verser à la seconde personne une indemnité pour la perte visée au paragraphe (1), il peut rendre l'ordonnance qu'il juge indiquée pour accorder réparation par recouvrement de dommages-intérêts à l'égard de cette perte.

(5) In assessing the amount of compensation the court shall take into account all matters that it considers relevant to the assessment of the amount, including any conduct of the first or second person which contributed to delay the disposition of the application under subsection 6(1).

(5) Pour déterminer le montant de l'indemnité à accorder, le tribunal tient compte des facteurs qu'il juge pertinents à cette fin, y compris, le cas échéant, la conduite de la première personne ou de la seconde personne qui a contribué à retarder le règlement de la demande visée au paragraphe 6(1).

(6) The Minister is not liable for damages under this section.

(6) Le ministre ne peut être tenu pour responsable des dommages-intérêts au titre du présent article.

[201] The above provision was considered in somewhat similar circumstances in Apotex Inc v Merck & Co, Inc, 2011 FCA 364, 430 NR 74 [Lovastatin 2011]. In that case Merck pleaded ex turpi causa actio non oritur in the context of Apotex's claim under section 8. Merck's argument was that Apotex could not claim a loss that arose in connection with an act of infringement. In allowing the appeal Justice John Evans had this to say:

[36] I do not accept Merck's submission that the Court should read into this provision limiting words to the effect, "unless the second person's claim is based on the loss that is has suffered by being prevented from infringing the first person's patent earlier." The presumption against reading words into a statutory text may be rebutted when demanded by context and legislative objective. In my view, it is not necessary to read an ex turpi causa exception into subsection 8(1) in order to prevent patent infringers from unjustly recovering compensation from a first person.

[37] This is because subsection 8(5) confers a broad discretion on the court when assessing the amount of compensation that the second person must pay. It provides that the court "shall take into account all matters that it considers relevant to the assessment of the amount," including any conduct by either party that contributed to the delay in the disposition of the first person's application for prohibition. In my view, this provision enables the Court to determine in its discretion whether, and to what extent, a second person's claim for compensation should be reduced, or eliminated.

[38] The Court's broad discretion under subsection 8(5) allows it, when considering arguments based on ex turpi causa, to have regard to the factual situation in its entirety, including its nuances. In the present case, one such nuance is that not all the tablets sold by Apotex were found in the infringement action to contain lovastatin made by the infringing process. A court is likely to find it easier to apply the ex turpi causa principle through an exercise of judicial discretion than through the definition of liability. Discretion enables the court to assess the appropriate amount of compensation payable (including nil) in a manner that properly takes account of all the relevant facts.

[Emphasis added.]

[202] The discretion conferred upon the Court by subsection 8(5) must accordingly be exercised with due regard to all of the circumstances bearing on the claim.

[203] Apotex's claim to section 8 damages arose from a NOC proceeding heard initially by Justice John A O'Keefe in connection with AstraZeneca's 762 Patent. That patent covered a combination medication for omeprazole and an anti-bacterial agent. Justice O'Keefe dismissed AstraZeneca's application on the basis that it had failed to establish that the Apotex product would infringe: see AstraZeneca AB v Apotex Inc, 2004 FC 313, 33 CPR (4th) 97. It was from Justice O'Keefe's Judgment that Apotex then brought its action seeking section 8 losses in the proceeding now before me in Court file T-2300-05. That proceeding was first heard by Justice Roger Hughes in the early part of 2012 and his Judgment can be found at Apotex Inc v AstraZeneca Canada Inc, 2012 FC 559, 410 FTR 168.

[204] When Justice Hughes heard the matter he was aware of AstraZeneca's outstanding action against Apotex in Court file T-1409-04, alleging an infringement of the 693 Patent. Indeed, one of the issues presented jointly to Justice Hughes was the following:

5. Whether the alleged infringement of the '693 Patent is relevant in law, including whether it is relevant as a defence, to the section 8 claim of Apotex (including possible set-off of damages) (and if so, see para. 4 of Order of October 4, 2011)?

[205] In dealing with this issue Justice Hughes cited the Federal Court of Appeal decision in Lovastatin 2011, quoted above, and the United Kingdom High Court of Justice, Chancery Division, Patents Court decision in Les Laboratoires Servier v Apotex Inc, [2011] EWHC 730 [Servier trial]. Justice Hughes neatly summed up the trial holding in Servier in the following way:

[143] The question of ex turpi causa came before the United Kingdom High Court of Justice, Chancery Division, Patents Court in Les Laboratoires Servier v Apotex Inc, [2011] EWHC 730 (Pat), a decision given by Justice Arnold. In that case, Apotex had been prevented from selling perindopril in the United Kingdom by an interlocutory injunction given pending trial. Servier, who obtained the injunction, had given an undertaking as to damages. Apotex prevailed at trial and sought damages pursuant to the undertaking. Servier argued that Apotex could not have made and sold the product, in any event, since the product would have been made in Canada. The Federal Court of Canada (Snider J.,) had held that Apotex's product would infringe a valid Servier Canadian patent, hence it would be unlawful for Apotex to make and export the product from Canada (Laboratoires Servier v Apotex Inc, 2008 FC 825). Justice Arnold made an extensive review of the law of ex turpi causa and concluded that the unlawfulness as proven must be sufficiently serious before a person engages the ex turpi causa rule, and that such unlawfulness must be an activity personal to the claimant, not vicarious.

[206] Although noting that the Servier trial decision was overturned on appeal, Justice Hughes observed that Apotex made a concession in that case that "played a critical role in the reversal". By that concession Apotex agreed that its recovery of damages in the English proceeding must be reduced by any damages awarded to Servier in its Canadian infringement action (as an additional cost of manufacture). This allowance was said to serve the interests of comity and to ensure that Apotex was not overcompensated. Justice Hughes said that the Servier solution "accords with what may properly be done in the present situation". He then went on to say, at para 148:

... A Court hearing the pending infringement action, if it concludes that the patent is valid and has been infringed by Apotex in making the omeprazole drug that is the subject of these proceedings, can at that time craft a remedy that is appropriate, having in mind any compensation awarded in these proceedings. It would be unconscionable for the present proceedings to come to a halt or for this Court to refuse to award compensation simply because another action on another patent was pending. To do so would be simply to encourage such

actions to be brought. The best way to deal with the matter is as I have set out above.

[Emphasis added.]

[207] Justice Hughes summarized his finding on this issue in the following way:

FINDING: In the circumstances of this case, the ex turpi causa rule is not engaged; the future possibility of a finding of infringement is insufficient to engage that rule. The infringement action is not material to a determination under subsection 8(1) in this case.

[Emphasis added.]

[208] His Judgment was then stated as follows:

1. Apotex is entitled to be compensated for loss suffered by it by reason of the proceedings taken by AstraZeneca in T-2311-01 for the period from January 3, 2002 until December 30, 2003 under the provisions of subsection 8(1) of the NOC Regulations;

2. There is no basis for an exercise of judicial discretion under subsection 8(5) of the NOC Regulations to reduce or refuse an award of such compensation;

...

[209] AstraZeneca appealed Justice Hughes' Judgment raising, inter alia, the following issue:

1. Is it relevant to the section 8 claim that Astrazeneca has sued Apotex for infringement of the patent in issue and the infringement trial has not yet been completed?

[210] The Court of Appeal upheld Justice Hughes' Judgment on this point for the following reasons [see Astrazeneca Canada Inc v Apotex Inc, 2013 FCA 77, 444 NR 254]:

[4] The first question arose when Astrazeneca asked Justice Hughes to delay the determination of section 8 damages in this case because its claim against Apotex for damages for infringement has not yet been determined. We note the jurisprudence to the effect that in assessing section 8 damages, the judge has the discretion under subsection 8(5) to reduce the damages based on an argument of ex turpi causa which could include an infringement claim (Apotex Inc. v. Merck & Co. Inc., 2011 FCA 364, at paragraphs 36 to 38). In this case, however, there has been no judicial determination that Apotex has infringed the patent, or would have done so but for the mandatory statutory stay during the prohibition proceedings.

[5] Justice Hughes had the discretion to refuse the request of Astrazeneca to delay the proceedings, and he did so. We have not been persuaded that the record discloses any basis upon which this Court should intervene.

[6] The fundamental reason for Justice Hughes' decision on this point is stated as follows at paragraph 148 of his reasons:

A Court hearing the pending infringement action, if it concludes that the patent is valid and has been infringed by Apotex in making the omeprazole drug that is the subject of these proceedings, can at that time craft a remedy that is appropriate, having in mind any compensation awarded in these proceedings.

[7] We agree with this statement. It will be for the judge trying the infringement action to ensure that overall, taking both proceedings together, a party is compensated for its provable loss, if any, on proper principles, no more and no less.

[Emphasis added.]

[211] The above disposition did not end the matter. When this Court did make a finding of infringement against Apotex in Court files T-1409-04 and T-1890-11, AstraZeneca brought the matter back to Justice Hughes in Court file T-2300-05 on a motion to reconsider. What AstraZeneca was seeking was a qualification to Justice Hughes' initial Judgment directing the reference judge to have regard to the infringement finding in Court files T-1409-04 and T-1890-11 "to reduce or refuse an award of [...] compensation".

[212] Justice Hughes dismissed AstraZeneca's motion both because my Judgment was still on appeal and because the requested relief amounted to an inappropriate request under Rule 399 of Federal Courts Rules, SOR/98-106, to reverse the effect of his original Judgment.

[213] Once again AstraZeneca appealed and once again the appeal was dismissed [see Astrazeneca Canada Inc v Apotex Inc, 2016 FCA 194, [2016] FCJ No 759 (QL)]. In considering the effect of my intervening infringement finding on Apotex's claim under section 8 of the NOC Regulations, the Court of Appeal said this:

[9] One of the errors asserted on appeal by AstraZeneca was that Justice Hughes had erred in finding the pending infringement action to be irrelevant to the claim for damages under section 8 of the Regulations. This Court rejected AstraZeneca's argument, expressly affirming the correctness of the passage quoted above at paragraph 6 and characterizing the passage to have been the fundamental reason for Justice Hughes' decision. The Court went on to state that "[i]t will be for the judge trying the infringement action to ensure that overall, taking both proceedings together, a party is compensated for its provable loss, if any, on proper principles, no more and no less".

[10] It is in this context that AstraZeneca moved for variation of the May 11, 2012 judgment. The basis for its motion was a finding by Justice Barnes of the Federal Court in an action for patent infringement that Apotex had infringed certain claims of the '693 Patent (2015 FC 322 and 2015 FC 671). This finding was said by AstraZeneca to be a new matter that arose after the judgment of Justice Hughes in the section 8 proceeding.

[11] Two variations to the judgment were sought by AstraZeneca on the motion. The first variation sought to add a provision that when determining Apotex' entitlement to damages, the reference Judge may have regard to the judgment of Justice Barnes. The second variation would have reversed Justice Hughes' conclusion that there was no basis for an exercise of

discretion under subsection 8(5) of the Regulations to reduce or refuse compensation to Apotex. Instead, the judgment would provide that the reference Judge might have regard to the judgment of Justice Barnes when exercising discretion under subsection 8(5) of the Regulations.

[12] As noted above, Justice Hughes dismissed the motion for variation. He gave a number of reasons for his decision, only two of which need be dealt with on this appeal.

[13] Justice Hughes' principal reason for dismissing the motion was that in his original decision he had expressly considered the scenario where Apotex might later be found to have infringed another patent. Further, this Court had agreed with his conclusion that it would be for the Judge in the infringement action to ensure a party is neither over nor under compensated for its loss. Thus, Justice Hughes wrote the "only thing that has now happened is that the 'might happen' scenario considered by me and the Court of Appeal has become a reality. That makes no difference. The 'reality' has already been considered and a determination made. Nothing changes."

[14] I agree with Justice Hughes for the reason that he gave. Justice Barnes' finding of infringement of the '693 Patent is not a matter that arose or was discovered after Justice Hughes' judgment in the section 8 proceeding within the contemplation of Rule 399(2)(a). This finding is dispositive of the appeal.

[...]

[24] A final note. This appeal and motion highlight the difficulties that ensue when inconsistent findings are made in parallel infringement and section 8 proceedings. I can only repeat Justice Sharlow's admonition on the prior appeal to the effect that it will be for the Judge hearing "the infringement action to ensure that overall, taking both proceedings together, a party is compensated for its provable loss, if any, on proper principles, no more and no less."

[214] What I take from the above-noted statements and particularly those of the Federal Court of Appeal is that, as the section 8 reference Judge, I have the discretion to take into account the intervening infringement finding, among other relevant facts, and to craft an appropriate remedy.

[215] This is also consistent with the broad parameters of the discretion discussed in Lovastatin 2011, above.

[216] I do not accept that AstraZeneca's right to raise this issue against Apotex ought to be precluded because of the order in which these matters initially came before this Court. If Apotex would have been required to account for its infringement of the 693 Patent had that finding been made ahead of Justice Hughes' section 8 Judgment, there is no principled basis for foreclosing that result because the order of the outcomes was reversed.

[217] What I am left with is a situation where, in order to recover its "losses" from being barred from selling Apo-Omeprazole between January 3, 2002 to December 30, 2003 in the face of AstraZeneca's 762 Patent, Apotex necessarily had to infringe AstraZeneca's 693 Patent. Apotex's claim to section 8 losses is accordingly offset by the costs of the corresponding infringement or, as AstraZeneca put it – if Apotex had entered the market during the section 8 liability period, it would have been required to disgorge its profits to AstraZeneca.

[218] As the Federal Court of Appeal observed in Lovastatin 2011, above, it is unnecessary to apply the theory of illegality to resolve this issue. Indeed, the strict application of that principle could, in some cases, leave a party undercompensated. This was essentially the point being made by Lord Toulson of the United Kingdom Supreme Court in the ultimate appeal of the Servier trial decision (Les Laboratoires Servier v Apotex Inc, [2014] UKSC 55 [Servier UKSC]) in the following passages:

52. The order made by the Court of Appeal accords with Lord Diplock's method of assessment. As Etherton LJ explained in his judgment at para 88, its effect is to place Apotex in precisely the position in which it would have been if there had been no UK interlocutory injunction, and it does not offend comity with Canada. Apotex will recover whatever sum may be left after deducting, from the proceeds of the lost sales, both the costs of the sales and the amount for which it would have had to account to Servier in the Canadian proceedings by way of damages for patent infringement. The result, Etherton LJ said, would neither be offensive to comity with Canada nor infringe English public policy.

53. By contrast, the order sought by Servier would potentially place it in a better position than if it had not obtained the English injunction for which it gave a cross-undertaking. I use the word potentially, because it remains to be seen how the Canadian court will calculate damages for the infringement which led to UK sales by Apotex. It will be a simple matter to apply the same approach to the lost sales as the Canadian court will apply in relation to actual sales made by Apotex. The result may be that Apotex will be unable to establish any loss, after deduction of the damages which it would have had to pay in Canada, but that will depend on the outcome of the Canadian proceedings.

[...]

63. Cross-undertakings are a standard and valuable feature of litigation, particularly but not only in commercial litigation. There is a public interest in their enforceability in bona fide disputes. It saves the court from having to make a more detailed – and therefore time consuming and expensive – assessment of the merits at an interlocutory stage than might otherwise be necessary, since the cross-undertaking is designed to protect the defendant against the applicant gaining a financial advantage from obtaining an injunction which is later set aside on the claim failing. I cannot see a good public policy reason why Servier should be put in a better position than if the English injunction had not been granted, or why Apotex should be required to give greater credit to Servier on account of its breach of the Canadian patent than the amount assessed by the Canadian court as properly reflecting

that breach.

[219] It follows that Apotex is not entitled to recover under section 8 of the NOC Regulations because it suffered no loss by being kept out of the marketplace between January 3, 2002 and December 30, 2003.

IV. With Respect to Apotex's Profits From the Infringement of the 693 Patent, What Allowance Should be Made for Profits-On-Profits [220] The parties do not disagree that a profits-on-profits allowance should be applied to AstraZeneca's profits entitlement. They differ only as to the amount and method of calculating the rate. AstraZeneca seeks prime plus two percent compounded annually. Apotex argues for simple interest at the bank rate.

[221] The burden on this issue rests with Apotex: see Reading & Bates Construction Co v Baker Energy Resources Corp (1994), 58 CPR (3d) 359 at p 375, 175 NR 225 (FCA) [Reading & Bates FCA].

[222] An award of interest on profits is not a matter of complete discretion. Such a recovery represents an accounting for the additional profit the infringer made from the use of the wrongfully acquired funds: see Teledyne Industries, Inc v Lido Industrial Products Ltd (1982), 68 CPR (2d) 204 at p 226, [1982] FCJ No 1024 (QL) (FCTD).

[223] Where it is not possible to know precisely how the infringer put its profits to use, it will be assumed to have made "the most beneficial use of them": see Reading & Bates FCA at p 376 and Adir v Apotex Inc, 2015 FC 721 at para 146, 482 FTR 276 [Perindropril FC]. In that situation the Court will estimate the return based on relevant investment or borrowing proxies. Compounded interest is the presumptive approach: see Reading & Bates FCA at p 374.

[224] As with the situation in Perindropril FC, above, it is not possible on the evidence before me to know exactly how Apotex made use of the profits generated from the sales of Apo-Omeprazole. Apotex co-mingled the sales proceeds from all of its products and used those funds in the day-to-day operation of its business. Money also moved back and forth on a daily basis between Apotex and Apotex Pharmachem Holdings Inc.

[225] Neither Ms. Paula Frederick nor Mr. Howard Rosen provided much help in establishing a rate of return and each adopted a rate that favoured the party retaining them. There was some evidence produced about Apotex's cost of borrowing from third-party lenders, ||||||||||||||||||||||||
||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||. Paying down those loans appears not to have been a priority for Apotex.

[226] It is apparent from Apotex's balance sheets that a lot of its capital expenditures and research & development costs were paid for from cash generated from operations. The overall impression is that Apotex typically used its profits to successfully build the business over the relevant period of infringement.

[227] To the extent Apotex relies on financial interactions with related companies as proof of its return, I reject that approach. I do not accept that non-arms-length transactions between related businesses are useful in the assessment of an appropriate rate of return. That is so because the terms of such arrangements can be easily manipulated to favour one party over the other. For example, one party could easily underutilize its profits by transferring them to a related party at low or zero interest. Alternatively, one party could borrow money from the other at an exorbitant rate and artificially inflate its costs.

[228] The decision of my colleague Justice Jocelyne Gagné in Perindropril FC, above, provides useful guidance about how to best apply the authorities to a very similar set of facts. As with the case at hand, Justice Gagné could not trace the profits earned by Apotex from its sales of perindopril. She observed that most of the relevant authorities have used prime plus one or two percent as proxies for a return on profits. She also observed that Apotex operates in a highly profitable environment. In the result, she awarded the compounded prime rate against Apotex. She applied slightly higher rates to the award against Pharmachem, consistent with its higher costs of borrowing (prime plus one-half and prime plus one, both compounded).

[229] In my view the benchmark rate for profits-on-profits in cases like this one has consistently been set at the prime rate or slightly higher, compounded annually. On the other hand, there is very little recent authority utilizing a rate as high as prime plus two percent. In this case, I fix the rate at prime compounded annually.

A. Tax Effects on Profits-on-Profits [230] Ms. Frederick acknowledged in her report that a deduction for income tax would be warranted on her profits-on-profits assessment. Nevertheless, she made no adjustment for tax because Apotex did not disclose its income tax returns for the relevant period.

[231] Under cross-examination it was suggested to Ms. Frederick that she could have applied a stipulated corporate tax rate to obtain an appropriate adjustment. She disagreed, saying that Apotex operates in a complex tax environment where generous research and development tax credits are available and where assumptions are unwarranted [see Transcript pp 306-8].

[232] On this issue, I agree with Ms. Frederick. Apotex could have avoided any uncertainty by producing its tax returns and it declined to do so. This is not the first time Apotex has faced this problem. In Wellcome Foundation Ltd v Apotex Inc, [2001] 2 FC 618, 11 CPR (4th) 218 (CA), the Court observed at para 30 that Apotex “did not tender its income tax returns as evidence of tax paid”. Apotex’s financial statements were described as “merely projections” and inadequate substitutes. The Court went on to observe that, despite being aware of its potential liability, Apotex “had not maintained financial records in a way that made it clear what expenses could be attributed for its various product lines” (para 31). The same point applies to some of Apotex’s records produced in this case.

[233] In the result, I allow nothing as a tax adjustment on the award of profits on profits.

V. With Respect to the Infringement of the 693 Patent, What Allowance is Required Having Regard to the United States District Court Award For the Infringement of the United States 505 Patent And Apotex's Satisfaction of That Award [234] A remaining point of disagreement between the parties concerns the appropriate treatment of the District Court award to AstraZeneca for Apotex's infringement of the United States 505 Patent. The parties have resolved the accounting issues in relation to this issue but disagree as to the legal effect of the United States Judgment on AstraZeneca's recovery in these proceedings. The parties have presented four options for the Court's consideration, ranging from a disgorgement of all Apotex's United States export profits less the amount already paid in satisfaction of the United States Judgment to a nil recovery (beyond the amount already paid in the United States proceeding). The four recovery scenarios are the following:

- Scenario A – Apotex disgorges all U.S. export profits, less its portion of the U.S. Judgment.
- Scenario B – Apotex disgorges US export profits made after expiry of the U.S. patent, April 20, 2007.
- Scenario C – Apotex disgorges U.S. export profits made after expiry of the pediatric extension, October 20, 2007.
- Scenario D – Apotex does not disgorge any U.S. export profits.

[235] AstraZeneca seeks recovery under Scenario A while Apotex maintains that Scenario D is the legally correct approach. Scenarios B and C are put forward by Apotex only in the alternative to D. The parties have agreed to the amounts to be paid (if any) depending on the Court's determination of legal entitlement.

[236] Apotex's fundamental objection to paying further compensation for its United States sales is based on principles of cause of action estoppel (including the doctrine of election), issue estoppel and abuse of process. AstraZeneca contends that it is not legally precluded from obtaining a further recovery in these proceedings provided full credit is given for Apotex's payment in satisfaction of the United States Judgment (thereby eliminating any form of double recovery).

[237] The legal authorities cited by the parties do not clearly resolve the question of how this Court ought to treat the District Court award beyond the recognition that full credit is due for Apotex's payment in satisfaction of the United States Judgment. On that point, the parties are agreed. Apotex says that, having elected to pursue compensation in the United States, AstraZeneca cannot claim any shortfall in these proceedings. AstraZeneca asserts that there are no legal barriers to a full recovery for Apotex's infringement of the 693 Patent.

[238] Perhaps the closest Canadian authority touching on Apotex's res judicata argument is Apotex Inc v Sanofi–Aventis, 2011 FC 1486, 101 CPR (4th) 1. In that case Apotex asserted a settlement agreement of a United States action as a bar to recovery in an infringement action between the parties in Canada. Justice Richard Boivin rejected Apotex's contention that the settlement agreement was intended to apply to Canada. He also dealt with Apotex's res judicata and abuse of process arguments in the following way:

[284] Finally, the Court further recalls that Apotex also raised the defences of estoppel and abuse of process in reference to the Settlement Agreements.

[285] With respect to estoppel, Apotex submits that, under this principle, Sanofi is precluded from pursuing in this action what is, according to Apotex, a second claim for compensation in respect of the very same manufacture and sale of the U.S. APO-clopidogrel.

[286] Moreover, Apotex argues that the monetary judgment in the U.S. Clopidogrel Action was secured on the basis of a contractual arrangement between the parties pursuant to which they stipulated as to what is essentially a factual matter (the measure of Sanofi's "actual damages" in the event of a launch at risk by Apotex in the U.S. and subsequent finding that the '265 Patent was valid and infringed). It follows, says Apotex, that Sanofi would be claiming damages in Canada on the same pills that were sold in the U.S. and were the subject of a damages award by Justice Stein of the United States District Court – Southern District of New York.

[287] Apotex also submits that if Sanofi is able to obtain an accounting of profits, they will be able to recoup the 50% that they negotiated away in the March and May 2006 Agreements. Because Apotex claims to have proceeded to act in reliance of that stipulation, Apotex argues that Sanofi should be estopped from attempting to circumvent that stipulation.

[288] An estoppel defence operates to preclude a party from relitigating the same cause of action twice (Danyluk v Ainsworth Technologies Inc., 2001 SCC 44, [2001] 2 SCR 460, at paras 18 and 54). In Toronto (City) v Canadian Union of Public Employees (C.U.P.E.), Local 79, 2003 SCC 63, [2003] 3 SCR 77, at para 23, the Supreme Court of Canada held that three (3) preconditions must be met for estoppel to be successfully invoked:

[23] ...(1) the issue must be the same as the one decided in the prior decision; (2) the prior judicial decision must have been final; and (3) the parties to both proceedings must be the same, or their privies (Danyluk v Ainsworth Tech., 2001 SCC 44, [2001] 2 SCR 460, 2001 SCC 44, at para 25, per Binnie J.) The final requirement, known as "mutuality", has been largely abandoned in the United States and has been the subject of much academic and judicial debate there as well as in the United Kingdom and, to some extent, in this country. (See G.D. Watson, "Duplicative Litigation: Issue Estoppel, Abuse of Process and the Death of Mutuality" (1990), 69 Can. Bar. Rev. 623 at pp. 648-51.) ...

[289] Res judicata is essentially premised on the notion that a matter has already been adjudged and is founded on the principles that a party shall not be vexed twice for the same complaint and that there is a societal value in the finality and conclusiveness of judicial decisions (see Angle v Canada (Minister of National Revenue), [1975] 2 SCR 248, at para 267; CPU Options, Inc. v Milton (2006), 79 OR (3d) 365, at para 15 (SCJ)).

[290] Against this background, the Court is not able to accede to Apotex' alleged estoppel defence because the U.S. litigation and the Agreements simply did not deal with infringement or the validity of the '777 Patent. It is therefore not open for the Court to conclude that the issue is the same as the one decided in the Agreements. The Court accordingly agrees with Sanofi that, where the legal rights upon which a cause of action is based were not adjudicated in the previous proceeding, the estoppel principle does not apply.

[291] Apotex has also raised the issue of abuse of process. In common law, judges have an inherent and residual discretion to prevent an abuse of the Court's process (CUPE, above, at para 35). However, the Court has not been convinced that this case boils down to a question of abuse of process. On the basis of the evidence and for the reasons mentioned above, the Court remains unpersuaded that Sanofi is using the courts for an improper use and that the integrity of the court's process is at issue in this case.

[Emphasis added.]

[239] On appeal the Court declined to resolve the issue of whether the losses from the infringement of the United States and Canadian patents were the same and therefore barred from recovery by the rule against double recovery [see Sanofi-Aventis v Apotex Inc, 2013 FCA 186, 114 CPR (4th) 1]:

[115] I would agree that the equitable rule against double recovery would prevent Sanofi from recovering the same loss twice. To the extent that the sale of clopidogrel in the U.S. in breach of the '265 patent is the same loss as that incurred by Sanofi from Apotex's exportation of clopidogrel to the U.S. for sale there, Sanofi could only recover that loss once. I point out, however, that it has not been established to this point that the infringement of the '265 and '777 Patent by the exportation of clopidogrel to the U.S. are, in fact or in law, the same loss. Since the matter must be returned to the Trial Judge on the question of remedies, I will say no more about that question.

[240] Apotex's res judicata argument is not based on an assertion of any misconduct. Rather, it contends that a public policy principle is at stake such that AstraZeneca ought to be estopped from pursuing the same essential recovery in two places. In simple terms, Apotex says that by opting to claim a recovery in the United States AstraZeneca must now accept that award as full satisfaction of its entitlement from the infringement of the 693 Patent for Apotex's sales into the United States.

[241] Apotex relies for its argument on the holding of the British Columbia Supreme Court in JRT Nurseries Inc v 0843374 BC Ltd, 2016 BCSC 501, [2016] BCJ No 578 (QL) [JRT]. That case involved proceedings brought in Oregon and in British Columbia for the recovery of damages arising from a common set of facts. The case was first tried in Oregon where product liability damages were recovered. The plaintiff was not satisfied with the Oregon results, including the inability in that jurisdiction to recover pre-judgment interest, and it sought to retry the case in British Columbia claiming under the Sale of Goods Act, RSBC 1996, c 410. The British Columbia litigation was halted on the basis of cause of action estoppel. The Court determined that the litigation could not be salvaged by recasting the liability theory or by reference to juridical differences to recovery between Oregon and British Columbia. The Court concluded as follows:

[51] ... In this case, the plaintiffs claimed their entire loss in the Oregon proceedings. Consequently, this is not like Cuttell v Bentz (1985), 65 BCLR 273 (CA) where the loss claimed in the first proceeding was not the full loss suffered by the plaintiffs (see p 289). Here, the claim was for all of the damages the plaintiff suffered from the conduct of the defendants, including Terralink as agent of Sun-Gro. That claim was adjudicated, and the judgment was satisfied. There was no shortfall within the proper meaning of that term, whether arising from a rethinking of the claim, the denial of prejudgment interest, or compromise.

[242] Apotex argues that the same approach is required in this case. It says AstraZeneca is seeking to recover essentially the same amounts that were the subject of the United States litigation and for which full United States compensation has been awarded and paid. Like JRT, above, it should not be entitled to recast the claim in these subsequent proceedings.

[243] I am not convinced, however, that JRT, above, applies to the situation before me. That case involved a common set of facts and issues that were fully triable in either Oregon or British Columbia. The Court easily saw through the plaintiff's attempt to recast the cause of action to recover a perceived shortfall in the Oregon proceeding.

[244] In these proceedings the circumstances are different. Here, the causes of action in the two proceedings arose under different patents, involved distinct acts of infringement and were tried in jurisdictions where different substantive legal principles applied. It is particularly noteworthy that the approach to recovery in the United States involved a hypothetical license and the fixing of a reasonable royalty. In that country, a claim to the infringer's profits has been unavailable since 1946: see Allied Signal Inc v Du Pont Canada Inc (1995), 61 CPR (3d) 417 at p 445 fn 11, 184 NR 113 (FCA). The amount awarded to AstraZeneca by the District Court under its approach also fell well short of AstraZeneca's entitlement in Canada to Apotex's profits from its United States sales.

[245] I would add that there is not a perfect temporal correspondence between the acts of infringement in issue in the United States litigation and those in play in these proceedings. AstraZeneca's United States claim arose from the infringement of the 505 Patent – a claim that necessarily ended with the expiry of that patent on April 20, 2007. After that date

Apotex was no longer infringing the United States patent and no viable claim to further royalties could be determined by the United States courts. But Apotex continued to infringe the 693 Patent by making Apo-Omeprazole in Canada and by exporting that product into the United States at a considerable profit. That conduct constituted a separate cause of action for which compensation is payable in these proceedings. It cannot be the case that, by proceeding first in the United States, AstraZeneca should be taken to have abandoned its claim for ongoing Canadian infringement post-dating the expiry of the United States patent.

[246] It seems to me that Apotex's argument in this case is much the same as Servier's argument in Servier, above. The issue presented by that case was whether Apotex should be barred from recovering damages in the United Kingdom because of its corresponding infringement in Canada of a Canadian patent. Damages were claimed by Apotex in the United Kingdom proceeding under an undertaking by Servier in support of the grant of an interlocutory injunction and where the European patent was later held invalid. As above, Servier argued that Apotex could not recover damages based on the principle of illegality – that is to say, that Apotex's lawful sales in the United Kingdom were the result of its infringement of a Canadian patent. The effect of a finding of illegality would be to preclude any recovery by Apotex under Servier's undertaking, regardless of the amount otherwise due in the United Kingdom proceeding.

[247] By the time the case was heard, Apotex had conceded that its claim to damages in the United Kingdom should be reduced by the amount it was ultimately required to pay in satisfaction of its Canadian liability. If that amount was less than its United Kingdom damages, Apotex sought to make up the difference.

[248] On appeal, both the English Court of Appeal and the United Kingdom Supreme Court declined to apply the doctrine of illegality based, at least in part, on a concern that the result might leave Servier with a windfall at the expense of Apotex.

[249] This point is made in the following passages from the respective Judgments of Lord Sumption and Lord Toulson in Servier UKSC:

30. In my opinion, the illegality defence is not engaged by the consideration that Apotex's lost profits would have been made by selling product manufactured in Canada in breach of Servier's Canadian patent. A patent is of course a public grant of the state. But it does not follow that the public interest is engaged by a breach of the patentee's rights. The effect of the grant is simply to give rise to private rights of a character no different in principle from contractual rights or rights founded on breaches of statutory duty or other torts. The only relevant interest affected is that of the patentee, and that is sufficiently vindicated by the availability of damages for the infringements in Canada, which will be deducted from any recovery under Servier's undertaking in England. There is no public policy which could justify in addition the forfeiture of Apotex's rights.

[per Lord Sumption]

...

53. By contrast, the order sought by Servier would potentially place it in a better position than if it had not obtained the English injunction for which it gave a cross-undertaking. I use the word potentially, because it remains to be seen how the Canadian court will calculate damages for the infringement which led to UK sales by Apotex. It will be a simple matter to apply the same approach to the lost sales as the Canadian court will apply in relation to actual sales made by Apotex. The result may be that Apotex will be unable to establish any loss, after deduction of the damages which it would have had to pay in Canada, but that will depend on the outcome of the Canadian proceedings.

...

63. Cross-undertakings are a standard and valuable feature of litigation, particularly but not only in commercial litigation. There is a public interest in their enforceability in bona fide disputes. It saves the court from having to make a more detailed – and therefore time consuming and expensive – assessment of the merits at an interlocutory stage than might otherwise be necessary, since the cross-undertaking is designed to protect the defendant against the applicant gaining a financial advantage from obtaining an injunction which is later set aside on the claim failing. I cannot see a good public policy reason why Servier should be put in a better position than if the English injunction had not been granted, or why Apotex should be required to give greater credit to Servier on account of its breach of the Canadian patent than the amount assessed by the Canadian court as properly reflecting that breach.

[per Lord Toulson]

[250] One other relevant consideration applied by the English Court of Appeal, Civil Division, concerned the territorial reach of a patent [see Les Laboratoires Servier v Apotex Inc, [2012] EWCA Civ 593]. At paragraph 83 the Court noted that a patent has limited territorial reach for liability purposes; but that does not mean that a court cannot examine matters arising beyond the border insofar as they concerned compensation:

[83] Thirdly, it was common ground before us that sales made in the United Kingdom from goods manufactured in breach of the Canadian Patent were not and (but for the injunction) would not have been unlawful under either Canadian or United Kingdom law. That is because patents are territorial. In the words of Kitchin LJ in the course of submissions, the tort comes to an end at the border: comp. the Patents Act 1977s 60. That is reflected in the final injunction granted by the Canadian court in the Canadian proceedings, which prohibited Apotex from manufacturing, selling, offering for sale or otherwise dealing in prindopril [sic] products in Canada [emphasis added]. Whether or not damages flowing from infringement, or an account of profits for infringement, would involve any investigation of matters that occurred outside the jurisdiction is a quite separate issue. As the Judge noted (in 103 of his

judgment) Servier does not contend that Apotex's United Kingdom business in importing and selling perindopril erbumine was unlawful.

[251] The examination of extra-territorial matters including foreign judgments is accordingly required to ensure that double recovery for the same loss does not occur but, absent illegality, it goes no further than that.

[252] It seems to me that if concurrent actions are permissible in more than one jurisdiction and, indeed, are necessary to ensure complete recovery across jurisdictions, the concerns about forum shopping, finality and multiplicity of proceedings largely disappear. Indeed, concurrent infringement actions in different jurisdictions claiming under similar patents for losses that may overlap are not an uncommon occurrence. Because the laws and the available legal options for recovery for patent infringement will vary from place to place (including the chance of different outcomes), the strict application of res judicata in all its forms and abuse of process by re-litigation are to be generally avoided. What will always remain of concern are the avoidance of either excess or inadequate recovery and the need to respect foreign judgments to achieve an equitable result.

[253] In this case AstraZeneca will be deprived of a full recovery if Scenario D is applied. Giving that effect to AstraZeneca's claim would be to afford extra-territorial reach to the 505 Patent. I am, therefore, satisfied that Scenario A is the correct approach to the treatment of the District Court award.

VI. Disposition [254] For the foregoing reason, the Court makes the following declarations in response to the issues presented by the parties for determination:

(a) At no time during the infringing period did Apotex have an available NIA;

(b) Apotex is not entitled to any section 8 damages recovery;

(c) AstraZeneca is entitled to recover an amount for profits-on-profits at the prime rate compounded annually and without a deduction for tax effects; and

(d) AstraZeneca is entitled to fully recover its claim to Apotex's profits for United States sales under Scenario A.

[255] The issue of costs and any other matters requiring the Court's consideration in accordance with the streamlining agreement will be reserved pending further submissions from the parties.

JUDGMENT IN T-1409-04, T-1890-11 AND T-2300-05

THE COURT ADJUDGES AND DECLARES the following:

(a) At no time during the infringing period did Apotex have an available NIA;

(b) Apotex is not entitled to any section 8 damages recovery;

(c) AstraZeneca is entitled to recover an amount for profits-on-profits at the prime rate compounded annually and without a deduction for tax effects; and

(d) AstraZeneca is entitled to fully recover its claim to Apotex's profits for United States sales under Scenario A.

"R.L. Barnes"

Judge

FEDERAL COURT

SOLICITORS OF RECORD

DOCKET:

T-1409-04

STYLE OF CAUSE:

ASTRAZENECA CANADA INC AND AKTIEBOLAGET HASSLE v APOTEX INC

AND DOCKET:

T-1890-11

STYLE OF CAUSE:

ASTRAZENECA AB AND AKTIEBOLAGET HASSLE v APOTEX INC

AND DOCKET:

T-2300-05

STYLE OF CAUSE:

APOTEX INC v ASTRAZENECA CANADA INC

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BARNES J.

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[1] The changes are detailed under Tab A to Dr. Davies' Report of March 23, 2017 (Exhibit AZ 138).

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