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Citation: 2015 FC 751

Ottawa, Ontario, June 15, 2015

PRESENT: The Honourable Mr. Justice Barnes

BETWEEN:

TAKEDA CANADA INC. AND TAKEDA GMBH

Applicants

And

THE MINISTER OF HEALTH AND MYLAN PHARMACEUTICALS ULC

Respondents

PUBLIC JUDGMENT AND REASONS
(Confidential Judgment and Reasons issued June 15, 2015)

[1] In this proceeding Takeda Canada Inc. and Takeda GMBH [hereafter Takeda] seek an Order under the Patented Medicines [Notice of Compliance] Regulations prohibiting the Minister of Health [Minister] from issuing a Notice of Compliance [NOC] to Mylan Pharmaceuticals ULC [hereafter Mylan] for its proposed version of Takeda's branded medicine, TECTA.

[2] The patent in issue is Canadian Letters Patent No. 2,341,031 [the 031 Patent] claiming, among other things, the compound pantoprazole magnesium dihydrate. The 031 Patent was filed on August 12, 1999 claiming priority to August 18, 1998. Takeda is the owner of the patent.

[3] Pantoprazole magnesium was known in the prior art for use as a gastric acid inhibitor but, according to Takeda, the discovery of its dihydrate form to treat gastric acid disorders was novel and non-obvious.

[4] The inventive concept of the 031 Patent is not in dispute. It is the compound pantoprazole magnesium dihydrate to treat disorders of the stomach and intestine.

[5] Claim 1 is the principal claim in issue. It claims the compound pantoprazole magnesium dihydrate. Takeda also asserts Claims 2, 8, 9, and 10 to 21 but the validity of Claim 1 underlies all of the other asserted claims. Similarly, if Claim 1 is not infringed by the Mylan product none of the other claims of the Patent will be infringed.

[6] Mylan's Notice of Allegation [NOA] and its Abbreviated New Drug Submission [ANDS] assert that its proposed pantoprazole magnesium product does not infringe the 031 Patent because it is a hemipentahydrate and not a dihydrate. It is common ground that dihydrates and hemipentahydrates of pantoprazole magnesium are distinct crystal forms containing different amounts of crystal bound water. Accordingly, the issue of infringement turns on the characterization of the hydration state of Mylan's product.

[7] Mylan's NOA also raised a number of validity challenges to the 031 Patent some of which it has subsequently abandoned. For the purpose of this decision, it will be sufficient to address only the issue of anticipation.

I. Background Science

[8] Almost all of the matters of relevant scientific background are not in dispute.

[9] Many chemical species have the ability to crystallize into more than one crystal structure. This phenomenon is known as polymorphism. Different polymorphs of the same material will display different structures and this can lead to variations in solubility, dissolution rate and bioavailability. Pseudopolymorphism refers to the ability of certain chemical species to crystallize around a solvent such as water. When water is the solvent, the crystal form is referred to as a hydrate. There can be any number of hydration states for a given chemical species. When a hydrate contains two molecules of water to one molecule of the chemical species, it is characterized as a dihydrate. When the ratio is 5 to 2, the hydrate is said to be a hemipentahydrate.

[10] Pantoprazole magnesium is a magnesium salt of pantoprazole. Every molecule of pantoprazole magnesium is made up of two molecules of pantoprazole to one molecule of magnesium. The dihydrate form of pantoprazole magnesium incorporates two molecules of water into the crystal lattice for every molecule of pantoprazole magnesium. For the hemipentahydrate form the ratio is 2.5 to 1.

[11] Hydrates can typically be identified or characterized by a variety of methods including X-Ray Powder Diffraction [XRPD], Differential Scanning Calorimetry [DSC], Thermogravimetric analysis [TGA], Karl Fischer titration [KF] and melting point.

[12] XRPD involves the exposure of a test sample to x-rays and the recording of the diffraction pattern. In almost every case different polymorphs will give off unique x-ray diffraction patterns. Two samples exhibiting the same pattern will almost always be the same compound.

[13] DSC can also distinguish between different polymorphs or pseudopolymorphs. DSC measures the difference in energy or heat flow between a sample and a reference sample as the temperature is increased over time. If two samples exhibit materially different melting points, their structures will be different. This test will not always be helpful because heat can cause different hydrates to convert to the same crystal form before the common form melts. In such circumstances, the test cannot assist in the identification of the original crystal form.

[14] TGA and KF are methods of measuring the amount of solvent in a pseudopolymorph. TGA measures the weight differential of the sample as the solvent is driven off with heating. KF directly measures the water content of the sample. Both tests are subject to a margin of error and can be affected by the applied experimental conditions.

[15] Mylan's ANDS submitted to the Minister reports that its product was characterized by KF, TGA, XRPD and DSC and found to be a hemipentahydrate.

II. Person of Skill in the Art

[16] The parties agree the person of skill is a chemist or chemical engineer with experience working with and characterizing solid crystalline forms.

III. Construction

[17] It is necessary, of course, to construe the claims of a patent in a purposive way before considering their validity or whether they are infringed. This is done through the eyes of the notional person of skill in the art to which the patent pertains. Claims are to be considered in the context of the entire patent, being neither benevolent nor harsh. Experts may assist as to the technical meaning of terms and as to the state of the art at the material time, but ultimately construction is an issue of law for the Court to determine. Experts do not construe the patent claims; instead they assist the Court in doing so: see *Whirlpool Inc v Camco Inc*, 2000 SCC 67 at paras 43-45 and 57, [2000] 2 SCR 1067.

[18] The parties are in essential agreement about the construction of the relevant claims. All of the asserted claims include pantoprazole magnesium dihydrate. All of the experts in the case construed Claim 1 to include all polymorphic forms of pantoprazole magnesium dihydrate: see Dr. Myerson's first affidavit at para 2(b)(v); Dr. Atwood's affidavit at para 59; Dr. Cima's affidavit at para 81. In other words, the claimed compound is defined by its hydration state and not by its crystal structure *per se*. The effect of this construction is that Takeda is asserting a monopoly over every possible dihydrate form of pantoprazole magnesium to treat gastric acid disorders, whether or not they were known or could be predicted at the time of the invention.

This seemingly runs counter to the evidence of all of the experts that one cannot predict in advance whether other hydrous forms exist and finding such a form is inherently inventive. The experts also agree that the utility of an unknown hydrous form cannot be predicted in advance of its discovery.

[19] I have some reservations about whether the person of skill would interpret Claim 1 in this expansive way. Although on its face, Claim 1 is not confined to any particular dihydrate form, the 031 Patent teaches methods for obtaining particular dihydrate forms. It says nothing about whether other dihydrate forms are likely to exist, how they could be made, or whether they would be likely to be useful. It is also of some significance that the inventors made some effort to characterize the obtained compounds by disclosing their water content values and melting points. These stipulations seemingly belie the broad construction of Claim 1 proffered by the experts, and support Mylan's initial pre-hearing construction set out at page 20 of its NOA.

[20] In my view, the person of skill would be more likely to read Claim 1 to include only the dihydrate forms the inventors discovered. Nevertheless, the determinative issues in this case are not dependant on this point of construction and it is not necessary to finally resolve this point.

IV. Onus of Proof

[21] The 031 Patent is presumed to be valid. Mylan has the initial burden of adducing sufficient evidence to give its NOA invalidity allegations an air of reality; on the determinative issue of anticipation, it has met that burden. The ultimate burden of proof on this issue thus rests with Takeda to prove, on a balance of probabilities, that Mylan's anticipation allegation is not

justified. On the issue of infringement, the burden rests on Takeda, on a balance of probabilities, to show that the Mylan product infringes. Evidence establishing only a possibility of infringement is insufficient to discharge this burden: see *Pfizer Canada Inc v Novophram Ltd*, 2005 FCA 270 at paras 24 and 28, 2005 FCA 270.

V. The Expert Witnesses

[22] Takeda relies on the evidence of Dr. Allan Myerson. Dr. Myerson is a Professor of the Practice in the Department of Chemical Engineering at the Massachusetts Institute of Technology [MIT]. He is a chemical engineer by training and has a 30-year history of working in the field of industrial crystallization. Much of his current research focus and professional writing concerns crystallization processes including novel formulation development and pharmaceutical manufacturing.

[23] Mylan relies on the evidence of Dr. Michael Cima and Dr. Jerry Atwood. Ironically, Dr. Cima works along-side Dr. Myerson at MIT. Dr. Cima has written extensively in the field of materials processing with particular emphasis on the discovery of novel crystal forms and formulations of pharmaceuticals. Dr. Atwood is the Chair of the Department of Chemistry at the University of Missouri-Columbia. He has considerable experience in the area of crystal growth and crystal engineering. He, too, is widely published and has served in an editorial capacity for several subject-related journals.

[24] All of these experts are well-qualified to express the opinions they gave in this proceeding. I can identify nothing about their respective backgrounds or conduct that would

undermine their opinion evidence. In particular, I reject Takeda's argument that Dr. Atwood was somehow tainted by prior exposure to Mylan's NOA before conducting his testing. There is, quite simply, no evidence that his experimental techniques were biased because of his background knowledge. Dr. Atwood explained his methods and disclosed his findings all of which were then open to scrutiny.

[25] There is nothing in the evidence that remotely supports the argument that Dr. Atwood's methodological choices were inherently inappropriate or calculated to obtain a pre-determined outcome. Indeed, Takeda elected not to conduct any testing of its own to directly challenge Dr. Atwood's data and Dr. Myerson failed to identify any step taken by Dr. Atwood which would be expected to obtain a result favourable to Mylan's position.

VI. Anticipation – What Does Example 10 of WO 114 Teach the Person of Skill?

[26] Mylan relies for its anticipation case on International Patent Application WO 97/41114 [WO 114] filed on April 22, 1997. WO 114 describes a process for preparing magnesium salts of certain benzimidazoles, including pantoprazole, known to be useful as gastric acid inhibitors. The 031 Patent acknowledges WO 114 as relevant prior art concerning the magnesium salt of pantoprazole but distinguishes the resulting product as an anhydrous form. Mylan and its experts say that Example 10 of the WO 114 necessarily produces pantoprazole magnesium dihydrate and it, therefore, anticipates the subject matter of the 031 Patent claims in issue.

[27] The point of disagreement between the parties is whether, by following Example 10 of WO 114, the inevitable result is pantoprazole magnesium dihydrate. The parties also disagree

about whether WO 114, on its face, teaches the person of skill that the resulting product of Example 10 will be an anhydrous form or a dihydrate form.

[28] WO 114 does not explicitly disclose to the person of skill whether the pantoprazole magnesium compound it produces is in any particular anhydrous or hydrous form. Clearly, there is nothing in this document tending to indicate that a dihydrate form is produced. At best, there are arguments suggesting that either an anhydrous or an unspecified hydrous form is produced.

[29] I do not agree with Dr. Myerson that the absence of a reference to water in the disclosed chemical formula is a compelling consideration. This could just as easily be explained by the inventors' indifference to the hydration state of the pantoprazole magnesium compound they obtained.

[30] I also do not accept that the person of skill would characterize the hydration state of this compound by relying solely on the stated values for theoretical and found magnesium content. Both Dr. Cima and Dr. Atwood say the reported value for found magnesium in Example 10 was within the margin of error for both anhydrous and dihydrous forms of pantoprazole magnesium. Dr. Myerson did not disagree that experimental error should be taken into account. He did not agree, however, that it would be considered by the person of skill to be as high as the value asserted by Dr. Atwood (±0.4%).

[31] Dr. Myerson took issue with Dr. Cima's statement that the actual magnesium content reported in Example 10 "falls well within the range, with margin of error, for both a dihydrate

and an anhydrous form of pantoprazole magnesium". Based on Dr. Cima's failure to identify the standard margin of error to be applied to the magnesium content value produced by Example 10, Dr. Myerson described Dr. Cima's conclusion as "unfounded". This criticism is substantially undermined by Dr. Myerson's own failure to state a value for the appropriate margin of error. In the absence of this information, Dr. Myerson concluded with the following largely unhelpful generalization:

> 121. The skilled chemist would not ignore the information in Example 10 that an anhydrous form of pantoprazole magnesium was prepared based on the potential experimental error in the found magnesium content.

[32] Considering the paucity of the evidence presented, I do not believe the person of skill would, by reading the WO 114 and applying common general knowledge, draw any conclusions about the hydration state of the pantoprazole magnesium compound produced by Example 10. Rather, the person of skill would follow the described process and, if desired, properly characterize the obtained compound by applying well-known and reliable techniques.

[33] I, therefore, agree with Takeda that, on its face, WO 114 does not inform the person of skill that the compound produced by Example 10 will be pantoprazole magnesium dihydrate or, indeed, any other particular hydrous form. At the same time it does not teach the person of skill that an anhydrous form will be obtained. The question remains, though, whether by following the process described in Example 10, the person of skill inevitably or necessarily obtains pantoprazole magnesium dihydrate.

[34] The law of anticipation applying to this question is well settled and was thoroughly summarized by Justice Roger Hughes in *Eli Lilly Canada Inc v Apotex Inc*, 2008 FC 142 at paras 145-149, [2008] FCJ No 171:

> [145] Lord Hoffman in the *Synthon* case, subsequent to *Merrell Dow* gave further consideration to the question of anticipation. In that case SmithKline had a patent which claimed a medicine called paroxetine methanesulfonate in a very particular crystalline form. A previous patent application published by Synthon disclosed a method for making paroxetine methanesulfonate but made no reference to any particular crystalline form. The evidence showed that if one were to follow the Synthon method, the particular SmithKline form would be made. Lord Hoffman therefore had to discuss anticipation from the perspective of the disclosure and enablement. He discussed *Merrell Dow* in this context at paragraphs 22 and 23 of *Synthon*:
>
> > *22. If I may summarise the effect of these two well-known statements, the matter relied upon as prior art must disclose subject-matter which, if performed, would necessarily result in an infringement of the patent. That may be because the prior art discloses the same invention. In that case there will be no question that performance of the earlier invention would infringe and usually it will be apparent to someone who is aware of both the prior art and the patent that it will do so. But patent infringement does not require that one should be aware that one is infringing: "whether or not a person is working [an] ... invention is an objective fact independent of what he knows or thinks about what he is doing": Merrell Dow Pharmaceuticals Inc v H N Norton & Co Ltd [1996] RPC 76, 90. It follows that, whether or not it would be apparent to anyone at the time, whenever subject-matter described in the prior disclosure is capable of being performed and is such that, if performed, it must result in the patent being infringed, the disclosure condition is satisfied. The flag has been planted, even though the author or maker of the prior art was not aware that he was doing so.*
> >
> > *23. Thus, in Merrell Dow, the ingestion of terfenadine by hay-fever sufferers, which was the subject of prior disclosure, necessarily entailed the*

> *making of the patented acid metabolite in their livers. It was therefore an anticipation of the acid metabolite, even though no one was aware that it was being made or even that it existed. But the infringement must be not merely a possible or even likely consequence of performing the invention disclosed by the prior disclosure. It must be necessarily entailed. If there is more than one possible consequence, one cannot say that performing the disclosed invention will infringe. The flag has not been planted on the patented invention, although a person performing the invention disclosed by the prior art may carry it there by accident or (if he is aware of the patented invention) by design. Indeed, it may be obvious to do so. But the prior disclosure must be construed as it would have been understood by the skilled person at the date of the disclosure and not in the light of the subsequent patent. As the Technical Board of Appeal said in T/396/89 UNION CARBIDE/high tear strength polymers [1992] EPOR 312 at para 4.4:*
>
> > *"It may be easy, given a knowledge of a later invention, to select from the general teachings of a prior art document certain conditions, and apply them to an example in that document, so as to produce an end result having all the features of the later claim. However, success in so doing does not prove that the result was inevitable. All that it demonstrates is that, given knowledge of the later invention, the earlier teaching is capable of being adapted to give the same result. Such an adaptation cannot be used to attack the novelty of a later patent."*

[146] The *Synthon* reasons subsequently considered enablement beginning at paragraph 26 where Lord Hoffman said:

> *Enablement means that the ordinary skilled person would have been able to perform the invention which satisfies the requirement of disclosure.*

[147] At paragraph 28, Lord Hoffman warned:

> *It is very important to keep in mind that disclosure and enablement are distinct concepts, each of which has to be satisfied and each of which has its own rules.*

[148] He cited in paragraph 28 a decision of Laddie J. in which that judge said:

> *The requirement to include an enabling disclosure is concerned with teaching the public how the invention works, not devising the invention in the first place.*

[149] Then, Lord Hoffman considered the question as to whether one must, as he put it, necessarily infringe, in light of Merrell Dow in paragraph 33 of his Reasons:

> *There is also a danger of confusion in a case like Merrell Dow Pharmaceuticals Inc v H N Norton & Co Ltd [1996] RPC 76, in which the subject-matter disclosed in the prior art is not the same as the claimed invention but will, if performed, necessarily infringe. To satisfy the requirement of disclosure, it must be shown that there will necessarily be infringement of the patented invention. But the invention which must be enabled is the one disclosed by the prior art. It makes no sense to inquire as to whether the prior disclosure enables the skilled person to perform the patented invention, since ex hypothesi in such a case the skilled person will not even realise that he is doing so. Thus in Merrell Dow the question of enablement turned on whether the disclosure enabled the skilled man to make terfenadine and feed it to hay-fever sufferers, not on whether it enabled him to make the acid metabolite.*

[35] In *AstraZenaca Canada Inc v Apotex Inc*, 2010 FC 714, [2010] FCJ No 1014, Justice Hughes noted the variations in language sometimes employed around the legal test for so-called inherent anticipation. Nevertheless, it was unnecessary for him to sort out those

differences because, in the case before him, the prior art "would at best only occasionally result in the [claimed] product" and was not thus anticipatory [see para 125].

[36] More recently in *Synthon BV v Teva Pharmaceutical Industries Limited*, [2015] EWHC 1395 (Pat), [2015] All ER (D) 200 (May) , Justice Birss dealt with the issue of novelty in the context of choices left to the person of skill in carrying out prior art. His comments at para 89 are helpful:

> 89. There is no issue about enablement in this case, the question arising over the Lemmon prior art is about the first limb of ***Synthon***. The issue is whether the prior art would fall within the claims. The test is a strict one, as the flag planting metaphor employed by Sachs LJ was intended to indicate. The test is one of necessity and inevitability. If a prior document leaves a choice open for the skilled person and if the result only falls within the patent claim if the skilled person adopts one way forward and not the other, then there is no lack of novelty. In that circumstance evidence that a skilled person "would" do something when faced with that choice is evidence relevant to obviousness, not novelty. The claim may lack inventive step but it has not been anticipated. On the other hand patentees will sometimes argue that a choice exists when in fact there is no genuine choice and in fact the patented way forward really is inevitable. If those are the facts then the claim lacks novelty but that is not because the skilled person had to make a choice, it is because there really was no choice at all. Fanciful supposed choices do not count.

[37] In *Abbott Laboratories v Sandoz Canada Inc*, 2008 FC 1359 aff'd 2009 FCA 94, [2009] FCJ No 345 , Justice Hughes summarized the law of anticipation into the following seven points:

> 1. For there to be anticipation there must be both disclosure and enablement of the claimed invention.
>
> 2. The disclosure does not have to be an "exact description" of the claimed invention. The disclosure must be sufficient so that when read by a person skilled in the art willing to understand what is being said, it can be understood without trial and error.

> 3. If there is sufficient disclosure, what is disclosed must enable a person skilled in the art to carry out what is disclosed. A certain amount of trial and error experimentation of a kind normally expected may be carried out.
>
> 4. The disclosure when carried out may be done without a person necessarily recognizing what is present or what is happening.
>
> 5. If the claimed invention is directed to a use different from that previously disclosed and enabled then such claimed use is not anticipated. However if the claimed use is the same as the previously disclosed and enabled use, then there is anticipation.
>
> 6. The Court is required to make its determinations as to disclosure and enablement on the usual civil burden of balance and probabilities, and not to any more exacting standard such as quasi-criminal.
>
> 7. If a person carrying out the prior disclosure would infringe the claim then the claim is anticipated.

[38] In *Apotex Inc v Sanofi-Synthelabo Canada Inc*, 2008 SCC 61, [2008] 3 SCR 265, the Court discussed the requirement for enablement. In attempting to put the prior art into practice, the person of skill is entitled to carry out routine trial and error experimentation including the application of common general knowledge. The amount of work required cannot constitute an undue burden but errors or omissions in the prior art reference may be overcome if the person of skill could readily correct the error or find what was omitted.

[39] Applying the above principles to this proceeding, the 031 Patent claims in issue will not be anticipated if, on a balance of probabilities, Takeda can show that following Example 10 of WO 114 does not inevitably or necessarily produce pantoprazole magnesium dihydrate. If the evidence discloses on a balance of probabilities only that a dihydrate will sometimes be the result, Takeda will have met its burden.

[40] The only direct evidence of what Example 10 of WO 114 produces comes from Dr. Atwood. According to Dr. Atwood, he followed the exemplified process and obtained a compound that he characterized by XRPD, DSC and TGA as pantoprazole magnesium dihydrate. The XRPD pattern he obtained matched one from US 623 for a dihydrate, and the melting point and water content data he obtained corresponded closely to the characterization data disclosed in the 031 Patent. In particular, the water content value obtained by TGA was 4.43% as compared to the theoretical loss of bound water expected for pantoprazole magnesium dihydrate of 4.37%.

[41] Dr. Myerson did not attempt to replicate Example 10 of WO 114 nor did he purport to challenge Dr. Atwood's characterization of the compound he made as pantoprazole magnesium dihydrate. Instead Dr. Myerson took issue with Dr. Atwood's methods and experimental choices.

[42] Dr. Myerson expressed the view that Dr. Atwood could not have accurately replicated Example 10 because his experimental yield was only half of what WO 114 had reported. According to Dr. Myerson this indicated something was wrong with Dr. Atwood's experiment. The probable cause for the reduced yield was attributed to Dr. Atwood's supposed deviations from Example 10 for the addition of water. Dr. Myerson described the problem as follows:

> 128. Dr. Atwood's reduced yield can likely be traced to his not following the procedure as described in Example 10 of the 114 patent. The example indicates that water should be added dropwise and the solution should be held for 30 minutes after the end of the water addition. In contrast, Dr. Atwood added the water over 30 minutes and then immediately isolated the solution. This changed process appears to have isolated the product while the solution was far from equilibrium thus resulting in his reduced yield. Reducing this yield will potentially change the solid form obtained.
>
> 129. Dr. Atwood's procedure also resulted in a very different saturation profile (crystallization driving force). Higher

> supersaturation profiles are well known to have the potential of producing different crystalline forms when compared to lower supersaturation profiles. Supersaturation profile is well known to influence a solid form obtained as is isolating a solid when the system is still far from equilibrium.
>
> 130. These deviations from the actual procedures of Example 10 of the 114 application indicate that Dr. Atwood's procedure was not an accurate reproduction of this procedure.

[43] Dr. Myerson also noted that it was necessary for Dr. Atwood to fill in some testing gaps concerned with drying time and temperature and the rate for adding water. According to Dr. Myerson, changes to these experimental choices could result in a compound with a different hydration state. Various passages in Dr. Myerson's affidavit describe this potential in different ways: eg: "can have a significant impact on the resulting product", "would likely affect the process and the resulting product", "the rate of addition of water can affect the crystallization process and the hydration level of any resulting crystalline product", "reducing this yield will potentially change the solid form obtained".

[44] Dr. Myerson concluded that Dr. Atwood's experimental choices and errors were sufficiently material to the outcome that a person of skill following Example 10 but adopting a different approach, would not expect to always obtain the same result.

[45] Dr. Myerson concluded his anticipation opinion in the following way:

> 139. In light of the above, it is my opinion that the 114 Application does not disclose the pantoprazole magnesium dihydrate claimed in the 031 Patent nor does it disclose a process that necessarily makes such a hydrate.
>
> 140. I understand that, based on my opinion that the 114 Application does not satisfy the disclosure prong of

> anticipation, it is unnecessary for me to address the enablement prong.

[46] Dr. Cima's contribution to this issue included corroboration of the characterization of the product Dr. Atwood obtained as pantoprazole magnesium dihydrate. Dr. Cima also verified Dr. Atwood's experimental approach. Dr. Cima's affidavit offers the following concluding opinion:

> 154. Example 10 of the 114 Application disclosed the subject-matter of claim 1 and enabled the POSITA to practice the subject-matter of claim 1. The POSITA could follow what was taught in Example 10 and arrive at the subject-matter of claim 1, namely pantoprazole magnesium dihydrate, as simply and as easily as Dr. Atwood did. Having reviewed Dr. Atwood's experiment, I conclude that he employed no more than the common general knowledge of the skilled person in following the instructions of the 114 Application.
>
> 155. In addition, the 114 Application disclosed that the pantoprazole magnesium dihydrate produced in Example 10 was stable, useful as an inhibitor of gastric acid secretion and suitable to make pharmaceutical formulations such as tables (see page 1, lines 14-17 and page 2, lines 16-20 of the 114 Application). This additional disclosure anticipates claims 2 and 8 to 21 of the 031 Patent because it disclosed and enabled the subject-matter of claims 2 and 8 to 21 of the 031 Patent.
>
> 156. Furthermore, Example 10 disclosed a process in which pantoprazole was reacted with the magnesium salt, magnesium sulfate, in an aqueous solvent (*i.e.*, water). Therefore, Example 10 also anticipates claim 36 of the 031 Patent because it disclosed and enabled the subject-matter of claim 36. For all of these reasons, I conclude that the 114 Application anticipates the 031 Patent.
>
> [Footnotes omitted]

[47] I am satisfied on the evidence before me that Dr. Atwood followed the process described in Example 10 of the WO 114 and made reasonable and routine experimental choices where it

was necessary to do so. I am also satisfied that the compound he obtained was pantoprazole magnesium dihydrate. This still leaves for determination how probable it is that by making different choices a person of skill would, by following Example 10, obtain something other than a dihydrate.

[48] Dr. Myerson's stated concerns are all theoretical. Nowhere in his evidence does he state that by applying different drying methods or by taking different approaches to the addition of water, something other than a dihydrate would be the likely result. At most, he says that a different hydrous form might or could be obtained.

[49] It was, of course, open to Dr. Myerson to run his own experiment using his preferred methods, and to characterize the hydration state of the resulting compound. Presumably he was directed by Takeda not to take that step. Instead Dr. Myerson raised only theoretical concerns about Dr. Atwood's methods without saying how those choices would be likely to produce something other than a dihydrate. In *AstraZeneca Canada Inc v Apotex Inc*, 2015 FC 322, 252 ACWS (3d) 567, I expressed some reservation about that type of strategic choice:

> [361] The fact that a party may not agree with a chosen experimental design is not an excuse for failing to replicate the work to test the reliability of the reported data. The same applies to criticisms about the testing techniques employed by an opposing expert witness. An argument that other tests or controls could have been used loses much of its strength where a party chooses not to employ those same suggested methods in its own responding analysis to see if the results differ.

I would add, in the face of Takeda's failure to conduct a single test, its concern that Dr. Atwood only ran one is somewhat of a dissimulation.

[50] It is also of some significance that Dr. Atwood was not cross-examined about Dr. Myerson's stated concerns and, thus, Takeda enjoyed the benefit of Dr. Myerson's views in the absence of effective reply.

[51] Dr. Myerson's concerns about Dr. Atwood's choices also stand in rather marked contrast to Dr. Myerson's testimony about the teaching of the 031 Patent. In that context, Dr. Myerson had no difficulty in filling in methodological gaps in the process described to arrive at pantoprazole magnesium dihydrate. In particular, he acknowledged the absence of specific instructions about the rate of addition of water containing magnesium salt. He also noted the absence of a processing temperature for the resulting solution and he assumed it to be room temperature (see p 4341). This is, of course, in contrast to Dr. Myerson's concern about Dr. Atwood's approach where, for the purpose of carrying out Example 10 of WO 114, he also ran the experiment at room temperature.

[52] In the absence of any test data to support Dr. Myerson's opinion and considering the reliable results obtained by Dr. Atwood as verified by Dr. Cima, I find that Takeda has not met its burden of showing that Mylan's anticipation allegation is unjustified.

VII. Does the Mylan Product Infringe?

[53] Mylan asserted in its Notice of Application [NOA] that its pantoprazole magnesium product does not infringe the 031 Patent because it produces a hemipentahydrate form of the compound and the Patent covers only dihydrate forms. If, indeed, the Mylan compound is

pantoprazole magnesium hemipentahydrate, it is common ground that it does not and will not infringe.

[54] Takeda's case for infringement rests on a number of evidentiary points. It relies on Mylan's product specification for water content in a range that, at the lower end, would capture dihydrate forms. It also argues for an inference that Mylan intends to make a dihydrate based on Mylan's unexplained alteration to its water content specification moving the acceptable range more closely to a dihydrate standard.

[55] Takeda also relies on Mylan's product analyses as disclosed to the Minister and says that, notwithstanding Mylan's contrary assurances, the data confirms the Mylan product is a dihydrate. Much of this argument is based on Takeda's interpretation of the test data measuring the water content of Mylan's product batches. According to this argument, these data also indicate the Mylan product is a dihydrate.

[56] Finally, Takeda contends that it was prevented from conducting its own testing of Mylan's product to conclusively characterize its hydration state such that any uncertainty ought to be resolved in its favour.

[57] The determinative infringement issue, then, is whether the Mylan product is pantoprazole magnesium hemipentahydrate as it contends, or pantoprazole magnesium dihydrate as covered by the claims of the 031 Patent.

VIII. The Mylan Specification

[58] I put very little stock in the evidentiary significance of the Mylan specification allowing for a water content in a range of [redacted]% to [redacted]% w/w. This range captures the theoretical water content for both the dihydrate and hemipentahydrate forms.

[59] Although Dr. Myerson stated at paragraph 76 of his first affidavit that this specification "requires" that the Mylan product contain pantoprazole magnesium dihydrate, elsewhere in his affidavit and under cross-examination, he acknowledged the specification did not go that far:

> 539 Q. Okay. But your evidence is not that the specification -- Mylan's specification prevents it from making a hemipentahydrate?
>
> A. What they—I guess I'm not sure of what you mean, that it prevents them from.
>
> 540 Q. Well, you said that the specification encompasses in your view both a dihydrate and a hemipentahydrate, correct?
>
> A. Well, the water content specification.
>
> 541 Q. That's correct.
>
> A. There's all I'm talking about. Not how they make it; just the water content specification.
>
> 542 Q. Well, we're talking about the whole specification of the product, including its XRPD, for example, right?
>
> A. Okay. I'm not talking about that either.
>
> I made a very precise statement that their product specification of the water content encompasses both a dihydrate and a hemipentahydrate.
>
> 543 Q. Right. So, conversely, Mylan's specification allows it to make a hemipentahydrate as far as water content is --

A. Meaning that if they made a hemipentahydrate it would fall within their specified water content range?

544 Q. Yes.

A. That's correct.

545 Q. Right. And Mylan has represented to Health Canada that it will make a hemipentahydrate, correct?

A. That's what it says.

[60] The fact that a product specification incorporates a range of values that permits different compounds to be produced says very little about what is actually produced.

[61] In spite of relying on Mylan's specification in support of his opinion that its product is a dihydrate, Dr. Myerson acknowledged the frailty of this type of evidence in the following passage at paragraph 104 of his second affidavit:

> For example, Mylan's specification requires:
>
> (b) a water content by Karl-Fischer titration been [redacted]% w/w and [redacted]% w/w, yet justifies this range only as "a moisture that *could* be present in the material." Mylan's justification does not address at all why a range which captures both a pantoprazole magnesium dihydrate and hemipentahydrate is appropriate to characterize the product as a hemipentahydrate;
>
> [Emphasis added]

[62] I take Takeda's point that Mylan did not disclose the reason for altering its product specification for water content at the low end of the acceptable range from [redacted]% to [redacted]%. However, given the evidentiary limitations inherent in NOC proceedings, Mylan was not required to offer an explanation for that change and I am not prepared to speculate about

its motivations. I, therefore, reject Dr. Myerson's unsupported and pejorative attribution at paragraph 83 of his first affidavit. Indeed, it would take far stronger evidence than this to support an inference that Mylan's disclosure about its product to the Minister was deceitful.

IX. Mylan's Product Testing

[63] The expert witnesses differed about the adequacy of the analytical tools used by Mylan to assess the water content of its product and to thereby accurately characterize its hydration state. The significance of Mylan's KF testing was a particular focus of their disagreement.

[64] Dr. Myerson expressed the opinion that the measurements Mylan obtained were sufficiently accurate to establish the Mylan product as a dihydrate. Drs. Cima and Atwood came to the conclusion that the totality of the analytical evidence showed the Mylan product to be a hemipentahydrate.

[65] It is common ground that pantoprazole magnesium dihydrate incorporates two molecules of water for every molecule of pantoprazole magnesium. The water is bound into the crystal lattice of the compound. This results in a theoretical bound water content of 4.37% w/w[1]. The experts also agree that the characterization of pantoprazole magnesium dihydrate cannot be confined to products with a precise water content of 4.37%. Rather, a range of water content values would be expected, taking account of experimental error including testing variables.

[1] For comparison a hemipentahydrate of pantoprazole magnesium contains 2.5 moles of water for every mole of pantoprazole magnesium with a theoretical water content of 5.40% w/w.

[66] Dr. Myerson relied heavily on Mylan's KF data measuring the water content of its product. According to Dr. Myerson the Certificates of Analysis produced by Mylan to the Minister for each of its four batches of pantoprazole magnesium product exhibited water content consistent with a dihydrate and not a hemipentahydrate. Those data consisted of the following water content values:

	Batch No.	**March 2012**	**April 2013**
(a)	25500700	[redacted]% w/w	[redacted]% w/w
(b)	25500701	[redacted]% w/w	[redacted]% w/w
(c)	25500769	[redacted]% w/w	[redacted]% w/w
(d)	25500771	[redacted]% w/w	[redacted]% w/w

[67] Dr. Myerson acknowledged these data all fell above the theoretical water content of pantoprazole magnesium dihydrate and below the theoretical water content of the hemipentahydrate form. Nevertheless, the April 2013 reported water values were closer to the theoretical value for a dihydrate than a hemipentahydrate, leading Dr. Myerson to conclude the Mylan product batches were dihydrates. This view, he said, was reinforced because it was more common for KF to overestimate the water content of a hydrated crystal form due to the presence of adventitious water. Nevertheless, he also acknowledged that KF can sometimes underestimate the water content of a sample when it has been over-dried.

[68] It is acknowledged by the experts that KF has inherent limitations as a means of precisely determining the bound water content of a crystal sample. A particular confounding variable with the use of KF is its inability to distinguish between adventitious (ie. free) water and bound water

in a test sample. KF measures all of the water in a sample but only the bound water content is relevant to the characterization of its hydration state. To isolate bound water content it is necessary to drive off the adventitious water and to measure what is left behind.

[69] Dr. Myerson acknowledged, to an extent, the imprecision associated with the measurement of bound water in a crystalline sample with KF. At paragraph 62(b)(iv) of his first affidavit, he recognized the existence of experimental error and the problem of removing residual adventitious water from a test sample. Although samples are usually pre-dried to drive off adventitious water, the process may either be incomplete or excessive resulting in KF measurements that are either "slightly higher" or "slightly below" the theoretical value for water content. According to Dr. Myerson, actual KF measurements ranging from 4.3% to 4.8% are consistent with the theoretical water content of pantoprazole magnesium dihydrate of 4.37%. It is on this point that Drs. Cima and Atwood parted company with Dr. Myerson.

[70] Dr. Atwood did not accept that KF on its own was sufficient to characterize the hydration state of pantoprazole magnesium. He made the point at paragraph 67 of his affidavit in the following way:

> 67. In my opinion, water content measurements of 4.3-4.8% alone, made via KF titration, would not inform the skilled person that a dihydrate of pantoprazole magnesium had been obtained. Further characterization would be required.

[71] Dr. Cima put the issue in a slightly different way. Although he agreed a dihydrate has one molecule of active compound for every two molecules of water, "each particular hydrate has

a range of water composition that can be tolerated without change in crystal structure" [see paras 30 and 124 of his affidavit].

[72] Despite his reliance on Mylan's KF data, Dr. Myerson did express some reservation about using a single method to characterize the hydration state of a crystal form in the following exchanges:

> 125 Q. What techniques are commonly use [sic] to characterize crystalline form?
>
> A. Well, clearly there's a whole series, but normally you would start with powder x-ray diffraction, differential scanning calorimetry, thermographic metric analysis.
>
> 126 Q. That's TGA, right?
>
> A. TGA, right. Yeah, I'll call those DSC and TGA as we go on since I've given the names, okay.
>
> 127 Q. Very well. And when you referred to powder x-ray diffraction, that's also sometimes called XRPD, right?
>
> A. Right
>
> 128 Q. Okay.
>
> A. We also routinely do Raman spectroscopy. Sometimes FTIR; that's Fourier Transform Infrared Spectroscopy. Occasionally solid-state NMR. Light microscopy, polarized light microscopy is something we typically do.
>
> That would be the -- the most common suite of things that we do in my lab
>
> 129 Q. Okay. And generally would those be the most common techniques beyond your lab, as well to characterize crystalline forms?
>
> A. Yes.
>
> …

> 406 Q. You -- you've taught a number of seminars, correct? Seminars about polymorphism, for example, or crystallization?
>
> A. I've been teaching crystallization short courses for the last 25 years.
>
> 407 Q. Excellent. And you don't teach to your students that a magnesium content test is a good test to determine the hydration state of a crystal form; do you?
>
> A, For determining the hydration state, I would normally tell them to do DSC, TGA, Karl Fischer analyses; and when necessary, I've talked to them about doing elemental analysis actually as a means of determining content.

[73] Mylan's product testing also included a water content analysis performed under TGA, which produced a value of [redacted]%. Dr. Myerson discounted this finding on the basis that it overestimated the weight loss due to dehydration by "approximately 1%". In the result, the loss of bound water "should be no more than [redacted]% in terms of the mass of hydrated water lost from the crystal" [see para 96 of his first affidavit]. Dr. Myerson supported this assessment by examining the DSC tracing produced by Mylan. From that tracing he identified the point of the onset of dehydration at "approximately 110ºC". Using this approach he estimated the correct starting weight percentage at 99% weight value resulting in an adjusted TGA value of [redacted]%. Under cross-examination he agreed the figure could be as high as [redacted]% [see p 4354].

[74] Although Dr. Cima agreed with Dr. Myerson that an allowance for the presence of adventitious water was appropriate, he disagreed that it would be as high as 1%. Based on a cited documentary reference, Dr. Cima concluded that an adjustment for adventitious water of up to 0.5% would be appropriate. This reduced the reported TGA value to no less than [redacted]%

– a value consistent with the theoretical water content of a hemipentahydrate. Dr. Cima also identified a particular concern about Dr. Myerson's working assumption that the loss of bound water in the Mylan sample all occurred at a temperature of 110ºC or higher. This point is addressed at paragraph 121 of his affidavit:

> 121. I disagree with Dr. Myerson when he states at paragraph 96 of his Affidavit that the amount of bound water lost from Mylan's product is [redacted]%. Dr. Myerson incorrectly assumes that only water lost at 110°C or higher is bound water. When a hydrate is heated, bound water is lost as soon as the equilibrium vapor pressure of water is disrupted by raising the temperature. Simply put, water is removed from the crystal structure as soon as the temperature is increased (see my discussion above). Lower temperatures, such as 50°C, are sufficient to remove bound water. For example, one can create an experiment where all of the bound water in a crystalline compound is removed by heating the compound to a mere 50°C for a long enough period of time. In fact, a TGA may be run at a constant temperature of 50°C, but conducting such a TGA would take much longer. The gradual increase in temperature to over 200°C allows a TGA test to be conducted much more quickly. Therefore, I disagree with Dr. Myerson's conclusion that only water lost from the Mylan Product at temperatures greater than 110°C is bound water.
>
> [Footnotes omitted]

[75] What these water content data indicate is a range of water content for the Mylan batch samples falling between the theoretical water content of the dihydrate and the hemipentahydrate. In some cases, the values are closer to the hemipentahydrate form while others are closer to the dihydrate form. Even Dr. Myerson obtained a TGA value falling slightly above the range he had set for characterization of the dihydrate form. In short, these results are, on their own, equivocal and insufficient to support a finding that the Mylan product is a dihydrate.

[76] There are some additional difficulties associated with Dr. Myerson's reliance on these water content data.

[77] Dr. Myerson did not specifically address Mylan's 2012 KF values for the same batches which, in three of the four cases, were closer to the theoretical water content of a hemipentahydrate and, in the fourth case, was effectively equidistant. This evidence did not, however, affect Dr. Myerson's opinion. At paragraph 90 of his affidavit, he stated:

> 90. I note that the modestly higher water contents determined during the original analysis of Mylan's four pantoprazole magnesium batches are all still well below the theoretical water content of pantoprazole magnesium hemipentahydrate. In my view, these earlier water content measurements also support my conclusion that the four batches were pantoprazole magnesium dihydrate.

In my view this type of analysis is largely unhelpful. If the data on their face do not support the opinion being advanced, it is not good enough to fall back on generalizations. The 2012 KF values may have been "modestly higher" than the 2013 results but the fact remains they were, in three of four cases, closer to the theoretical value of a hemipentahydrate than a dihydrate and, therefore, cannot be dismissed as readily as Dr. Myerson suggests.

[78] Dr. Myerson also failed to explain the water content disparities between 2012 and 2013 where for each batch, the KF values fell. In contrast, Dr. Cima explained why KF analysis can produce inaccurate results:

> 129. In these circumstances, I rely on Mylan's TGA results in preference to Mylan's KF results because TGA is generally more reliable than KF. There are several reasons why a KF may produce an erroneous water content reading, and relatively fewer reasons why a TGA might do so. For example, a KF test will be inaccurate

> if the compound is not completely dissolved during the test. In that case, not all of the water in the sample would be available and this problem would cause a KF test to underestimate a sample's water content.
>
> 130. KF is also susceptible to other errors. For example, the KF will produce erroneous water content readings if there is contamination, or if the reagents were made incorrectly, are too old or were loaded incorrectly. It is also known that many KF apparatuses are most reliable when used with material containing only a small percentage of water or when measuring a small amount of water, in absolute terms, from a sample. Based on the foregoing and given the inconsistency between Mylan's TGA and KF, I do not put stock in Mylan's KF results.
>
> [Footnotes omitted]

Also see the affidavit of Dr. Atwood at paragraphs 119, 129-130.

[79] It seems to me that there is considerable imprecision associated with the measurement of the bound water content of pseudopolymorphs under both KF and TGA analysis. The results are partly dependant on one's ability to accurately detect when adventitious water in a test sample has been completely removed and when dehydration of the crystal bound water begins. I accept Dr. Cima's evidence that there is no sharp point of demarcation and the loss of adventitious and bound water can overlap to some extent, thus making the required extrapolation more difficult.

[80] In addition there are other experimental variables which can affect the values obtained by KF and TGA analysis. Things like the failure to fully dissolve the tested compound may result in the under-reporting of water content by KF as noted above.

[81] I am not satisfied on the record before me that the KF and TGA data reported by Mylan support Dr. Myerson's opinion that the Mylan pantoprazole magnesium product is a dihydrate. The test results are equivocal and, to some extent, inconsistent. They are also subject to a degree of error and interpretive uncertainty. Even Dr. Myerson acknowledged additional tests to KF and TGA would typically be required to fully characterize the hydration state of a crystal form.

[82] Dr. Myerson summarily dismissed the relevance of Mylan's melting point analysis, stating it is unhelpful to the determination of a compound's hydration state [see para 100 of his first affidavit]. That point, in isolation, is undoubtedly correct but in this situation it fails to deal with the melting point data set out in the 031 Patent.

[83] At paragraph 107 of his affidavit Dr. Atwood points out the Mylan product was shown to have a melting point of [redacted]ºC as compared to the products in the 031 Patent which had reported melting points between 194-198ºC. According to Dr. Atwood, this differential was sufficient to show the compounds were different.

[84] Under cross-examination, Dr. Myerson said hydrates "don't have melting points". Instead they only have "dehydration temperatures" or "decomposition points". According to Dr. Myerson the description of melting points in the 031 Patent and the Mylan disclosure represented sloppy nomenclature. Nevertheless, he used the same term in paragraph 100 of his first affidavit.

[85] Dr. Myerson's attempt to discount the relevance of this data on highly technical grounds is not convincing.

[86] The 031 Patent characterized the obtained compounds with melting points in a range between 194ºC and 198ºC. These data were obtained with DSC analysis and were apparently thought by the inventors to be material to the characterization of their invented compounds. Mylan's DSC results disclosed a melting point of [redacted]ºC. I accept this difference does not disclose the hydration state of the tested compounds but it does indicate the Mylan compound is different from the compounds exemplified by the 031 Patent. Even Dr. Myerson seems to have acknowledged the potential significance of this evidence in the following exchange under cross-examination:

> 253 Q. The melting points that are reported in the example of the 031 patent are within 1 to 2 degrees?
>
> A. I believe -- I don't recall.
>
> 254 Q. Let's take a look at it.
>
> A. 90 – if we look at page3 --
>
> 255 Q. That's right.
>
> A. -- in the example, melting point, 194 to 196 was decomposition.
>
> 256 Q. Okay. That's one.
>
> A. So they're seeing the decomposition point.
>
> 257 Q. Look in Table 1, the melting points reported, 196 to 197; that's within 2 degrees?
>
> A. Oh, yes, so we have 196 to 197, 196 to 197, 197 to 198, and 195 to 196.
>
> 258 Q. Right. So these are all within 2 degrees; 2 degrees are reported for each one of these points?

A. That's correct.

259 Q. And those would be sharp points?

A. Yeah, they're sharp points. It's not surprising because they're decomposition points.

260 Q. If you have two samples of the same substance and each sample has a different melting point, those two samples must be different forms, correct?

A. Two samples of the same substance, if you put in the caveat that they have the same purity --

261 Q. Yes.

A. --and the same level of crystallinity, meaning that they're both highly crystalline --

262 Q. Yes.

A. -- if you have different melting points, they should be different forms, that's correct.

263 Q. They must be different forms, right?

A. That's right.

264 Q. You agree that different polymorphs have different melting points, correct?

A. Yes.

265 Q. You agree that melting points are used to characterize crystal forms of compounds as well as to indicate the chemical purity of these materials?

A. Correct.

266 Q. You agree that relatively pure solids generally have melting points within a range of approximately 1 degree when measured?

A. Correct.

267 Q. You agree that different polymorphs will have different melting points?

A. Yes.

> 268 Q. You agree that a melting point range of 1 degree Celsius is considered a relatively sharp melting point and would generally indicate a pure crystalline phase?
>
> A. Yes.
>
> 269 Q. You testified in the efavirenz case that a difference of 7 to 9 degrees in melting points was a substantial difference; do you remember that?
>
> A. Yes.
>
> 270 Q. And that was true?
>
> A. Yes.

[87] I accordingly reject Dr. Myerson's affidavit evidence that the melting point data were of no probative value in characterizing the Mylan product.

[88] A significant piece of evidence relied upon by Mylan to characterize its product as a hemipentahydrate arises from a comparative analysis of XRPD data. The XRPD pattern obtained by Mylan for its product matches the XRPD pattern reported in US 623 for [redacted----------] was characterized by the US 623 inventors as pantoprazole magnesium hemipentahydrate. As well, the XRPD pattern reported in US 623 for two dihydrate forms did not match the pattern for the Mylan product. Mylan uses [redacted------] as the reference standard for characterizing its product [see Application Record at p 2725].

[89] Relying on the correctness of the XRPD data reported in US 623, both Drs. Cima and Atwood concluded the Mylan product was a hemipentahydrate. Dr. Myerson also acknowledged where a crystalline form has been previously and unambiguously characterized by XRPD, the resulting pattern can be used as the sole means of subsequently verifying that form [see p 4327].

Dr. Myerson did not carry out a comparative analysis of the XRPD data and, in the result, the evidence of Drs. Cima and Atwood was left unchallenged.

[90] Takeda's only answer to this evidence is to attempt to block its introduction as inadmissible hearsay. I have no doubt this evidence is hearsay. Clearly Drs. Cima and Atwood based their opinions on the correctness of the characterization of [redacted] as a hemipentahydrate in US 623. If [redacted] was not a hemipentahydrate, as the inventors reported, those opinions are unsupported.

[91] Despite Mylan's argument, I do not believe this evidence falls clearly within one of the previously recognized exceptions to the hearsay rule. In particular, there is no evidence before me to show that the admission of this evidence was justified on the basis of its necessity. That said, the opinions expressed by expert witnesses in patent litigation frequently rest on their acceptance of the accuracy of hearsay references concerning scientific issues or for the interpretation of prior art. In some cases, this is justified on the ground that experts in a particular field are permitted to rely on the accuracy of widely accepted and publicly reported data.

[92] Given the summary nature of NOC proceedings, I am of the view that some latitude should be extended to the reliance by expert witnesses upon hearsay contained within authenticated and facially reliable scientific references. The contents of US 623 were disclosed in Mylan's NOA and its expert witnesses relied on the reported findings in support of their own analysis. Where such a reference contains sufficient information to allow the opposite party to

replicate the work and assess the accuracy of the reported data, that party suffers no material prejudice by the admission of hearsay in support of an expert's opinion. It was open to Takeda to run the same tests reported in US 623 and to fully characterize the resulting compounds. Despite the significance of this evidence, Takeda chose not to make that effort.

[93] This evidence, of course, strongly supports Mylan's representation to the Minister and to the Court that Mylan makes pantoprazole magnesium hemipentahydrate.

[94] Takeda also argues that it was unable to replicate Mylan's manufacturing process and it was not provided with a sample of the Mylan product. This left it without the means of independently characterizing the Mylan product – a disadvantage, it says, supports the drawing of an adverse inference against Mylan.

[95] Dr. Myerson reviewed the Mylan process parameters and concluded "that it cannot be replicated based solely on the information found in the Mylan Disclosure" [see para 2 of his first affidavit]. A particular concern identified by Dr. Myerson was the absence of information about [redacted----------].

[96] Whether or not Takeda had the ability to faithfully replicate the Mylan process or to obtain Mylan's exact seed material is not a complete answer to its ability to conduct relevant testing.

[97] Takeda was advised by counsel for Mylan in a formal response to requests for production that Mylan's product produces an XRPD pattern comparable to the XRPD pattern disclosed for [redacted] in US 623. Counsel's letter provided Takeda with the following information:

> In Tab 48, the Certificate of Analysis for the Reference Standard indicates that the X-ray diffraction pattern "should be comparable with pantoprazole magnesium hemipentahydrate". We have been informed by Mylan that the reference standard referred to in this document is the crystalline [redacted] exemplified in Figure [redacted] of U.S. Patent Application 2008/0139623 Al. We attach a copy of US 2008/0139623 Al for your convenience.

Takeda contends this is improper hearsay [see para 60 of Takeda's Memorandum of Fact and Law]. I do not understand this argument. When counsel, in fulfillment of a party's disclosure obligation, makes a representation, it is binding on the client. It would not have been open to Mylan to later disavow counsel's representation in the face of an attempt by Takeda to rely upon it.

[98] Mylan represented to the Minister that its product corresponds to a reference standard. Mylan told Takeda the reference standard it uses for XRPD comparison is that disclosed in US 623 as [redacted].

[99] It was thus open to Takeda to reproduce the US 623 process for making [redacted] and to fully characterize the obtained compound. If that characterization identified the compound as a dihydrate, and if its XRPD pattern corresponded to that for Mylan's product, a strong case for infringement would presumably be made out.

[100] On the question of Takeda's ability to carry out relevant testing seeking to corroborate Dr. Myerson's opinion, I prefer the evidence at paragraphs 140-144 of Dr. Atwood's affidavit:

> 140. I disagree with the statement by Dr. Myerson at paragraphs 113 to 118 of his affidavit that the Mylan process could not be replicated without the seed material.
>
> 141. Page 20 of the document at Tab 153 of Exhibit C to the Burkhardt Affidavit states, "Pantoprazole Magnesium Hemipentahydrate seed material is the approved batch of Pantoprazole Magnesium Hemipentahydrate meeting the specifications".
>
> 142. [redacted---------] US 623 provides a method to make 100% chemically pure pantoprazole magnesium [redacted] which is a hemipentahydrate and the comparator form for the Mylan-Pantoprazole-T hemipentahydrate, as explained in Exhibit I to the Burkhardt Affidavit. [redacted] does not require the use of a seed.
>
> 143. Had Dr. Myerson actually wanted to perform the Mylan process, he could have made a seed according to the process of [redacted-] of US 623 and then followed the process detailed at Tab 152 of Exhibit C to the Burkhardt Affidavit.
>
> 144. The disclosure of the Mylan process, together with the disclosure of the process in US 623 (which should have alerted Dr. Myerson that pantoprazole magnesium hemipentahydrate could be made with [redacted----------], shows that Dr. Myerson's could and should have been able to replicate Mylan's process and tested the product to determine it produced a hemipentahydrate.

Also see paragraph 138 of Dr. Cima's affidavit.

[101] I also do not accept Dr. Myerson's evidence that the absence of information in the Mylan disclosure about [redacted----------] rendered him incapable of replicating the Mylan process. Both Drs. Cima and Atwood noted the capacity of these compounds to [redacted----------]. US 623 also disclosed experimental methods for making hydrous forms of

pantoprazole magnesium where the [redacted----------]. Although Dr. Cima acknowledged it is unusual to rely on [redacted----------], the Mylan batch sizes were, according to him, [redacted----------].

[102] Against this background it was not enough for Dr. Myerson to predict failure without an attempt being made. If the process would not work, he was capable of showing that to be the case.

[103] In the face of Takeda's failure to take reasonable steps to independently verify Dr. Myerson's opinions, I am not prepared to draw an adverse inference against Mylan.

[104] In conclusion, Takeda has not met its burden of establishing that the Mylan product infringes the 031 Patent and this application is dismissed with costs payable to Mylan at the mid-point of Column IV.

X. Post-Script

[105] As with many NOC proceedings, this one produced several evidentiary gaps. Indeed, it is disconcerting that the parties to NOC proceedings often fail to test in a meaningful way the reliability of the opinions expressed by opposing expert witnesses. Instead the parties fall back on the largely unchallenged opinions of their own experts. In the result, the Court does not obtain the benefit of effective cross-examination on material issues of scientific disagreement or it is left to wonder on the validity of methodological criticism about otherwise unchallenged test data.

[106] This proceeding is a good example of that tendency. On some of the central issues of scientific disagreement among the three experts, no significant cross-examinations were conducted. This was particularly evident in Dr. Myerson's criticisms of Dr. Atwood's testing methods. Dr. Myerson identified certain theoretical weaknesses in Dr. Atwood's approach but Dr. Myerson was not directed to conduct his own testing using his preferred method to determine if different data emerged. Furthermore, Dr. Atwood was not cross-examined about Dr. Myerson's criticisms, presumably out of a concern that otherwise unavailable reply evidence could thereby enter the record. It is perhaps noteworthy that in one of the Prothonotary's Orders in this proceeding, a motion to file Reply evidence was refused partly in the expectation that the evidence would likely emerge under cross-examination.

[107] By their very nature, NOC proceedings allow for the possibility of evidentiary gaps. Reply evidence is often not permitted and product samples and other relevant evidence not contained within an ANDS filing is usually not discoverable. In this context, it does not assist the Court in getting to a just and accurate result by failing to effectively join issue on the conflicting opinion evidence which does enter the record.

JUDGMENT

THIS COURT'S JUDGMENT is that this application is dismissed with costs payable to Mylan at the mid-point of Column IV.

"R.L. Barnes"

Judge

FEDERAL COURT

SOLICITORS OF RECORD

DOCKET:	T-1161-13
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APPEARANCES:

Mr. Christopher Van Barr Mr. Kiernan A. Murphy Mr. William Boyer	FOR THE APPLICANTS
Mr. J. Bradley White Mr. Vincent M. de Grandpré Mr. Geoffrey Langen	FOR THE RESPONDENT MYLAN PHARMACEUTICALS ULC

SOLICITORS OF RECORD:

Gowling Lafleur Henderson LLP Ottawa, ON	FOR THE APPLICANTS
Osler, Hoskin & Harcourt LLP Ottawa, ON	FOR THE RESPONDENT
William F. Pentney Deputy Attorney General of Canada Toronto, ON	FOR THE RESPONDENT THE MINISTER OF HEALTH