Federal Court  Cour fédérale

Date: 20140113

Docket: T-278-12

Citation: 2014 FC 30

Ottawa, Ontario, January 13, 2014

PRESENT: The Honourable Mr. Justice Barnes

BETWEEN:

**BRISTOL-MYERS SQUIBB &
GILEAD SCIENCES, LLC AND
MERCK SHARP & DOHME CORP.**

Applicants

and

**TEVA CANADA LIMITED AND
THE MINISTER OF HEALTH**

Respondents

PUBLIC REASONS FOR JUDGMENT AND JUDGMENT

[1] This is an application by Bristol-Myers Squibb & Gilead Sciences, LLC and Merck Sharp & Dohme Corp. seeking an order under the *Patented Medicines (Notice of Compliance) Regulations*, SOR/93-133 as amended (PMNOC regulations) prohibiting the Minister of Health (Minister) from issuing a Notice of Compliance (NOC) to Teva Canada Limited (Teva) for a generic version of the Applicants' combination anti-retroviral medicine marketed under the brand Atripla. The Applicants

seek relief until the expiry of Canadian Letters Patent 2,279,198 (198 Patent) which expires on February 2, 2018.

[2] Merck is the owner of the 198 Patent and BMS and Gilead hold a joint venture license from Merck. Any reference hereafter to Merck will, unless otherwise indicated, include all of the Applicants.

[3] Teva served a Notice of Allegation (NOA) on December 22, 2011 asserting, *inter alia*, that the 198 Patent was invalid on numerous grounds including obviousness and anticipation. Teva also asserted that its proposed product will not infringe any of the claims of the 198 Patent.

[4] In the Notice of Application herein Merck relies only on Claims 1, 2 and 3 of 198 Patent. Merck maintains that those claims are valid and that the Teva product will infringe.

[5] This is the second proceeding that the Court has heard under the PMNOC regulations concerning the 198 Patent. In *Bristol-Myers Squibb Canada Co. v Mylan Pharmaceuticals ULC*, 2012 FC 1142, [2012] FCJ No 1251, the validity of the 198 Patent was upheld. Nevertheless, Mylan successfully defended the application on the ground that the Applicants had failed to establish an infringement. It is unnecessary on this occasion to repeat all of the background scientific points that were covered in those earlier reasons. Those matters are not the subject of controversy in this proceeding.

[6] A voluminous evidentiary record was developed by the parties in connection with the validity of the 198 Patent compound claims. Through no fault of the parties the Court has been left with a relatively brief period of time to comprehensively resolve all of the issues they have argued. Because the infringement issue is determinative, it is unnecessary and probably unwise to attempt to resolve the validity issues. I will say, however, that Teva presented a stronger case for invalidity on the ground of obviousness than was before me in the Mylan proceeding.

[7] The infringement issue in this proceeding concerns the likelihood that Teva's tablets will contain some amount of the compound claimed by the 198 Patent (ie. Form I efavirenz). It is common ground that Teva's starting medicinal compound (hereafter "Form Teva") does not contain Form I efavirenz. The question in dispute is whether Form Teva will convert in some measure to Form I during Teva's tablet manufacturing process.

[8] In order to avoid the potential for conversion, drug manufacturers usually prefer to use the most stable crystal form of a medicinal compound – provided, of course, that it fulfils the manufacturers' efficacy criteria. Faced with a patent on the most stable crystal form, generic manufacturers will sometimes use a less stable or metastable crystal form for the active medicinal compound and thereby attempt to avoid an infringement.

[9] Form I is the most stable crystal form of efavirenz and it is the subject of Claims 1, 2 and 3 of the 198 Patent. It is undisputed that, with the input of sufficient energy, all metastable crystal forms of efavirenz, including Form Teva, will convert to Form I.

[10] Teva's NOA asserts that Form Teva will not contain Form I and, therefore, will not infringe. The NOA acknowledgements that less stable crystal forms will "often" convert to a more stable crystal form, that Form I is the most stable crystal form of efavirenz and that "all other forms convert to Form I on heating" do not detract from Teva's fundamental assertion that, under the prevailing manufacturing and storage conditions, its product will not convert to Form I.

Issues

[11] Has Merck met its burden of proving that Teva's product will, in all probability, contain Form I efavirenz?

Analysis

[12] For the purposes of this decision, I adopt the legal principles set out in the Reasons for Judgment issued in *Bristol-Myers Squibb Canada Co. v Mylan Pharmaceuticals ULC*, above, and will not repeat them here.

[13] Merck led expert evidence from Dr. Allan Myerson in support of its case for infringement. Dr. Myerson, in turn, relied upon testing carried out by Dr. Mark Taylor at the University of Toronto. Dr. Taylor made a small quantity of Form Teva and, under the instructions of Dr. Myerson, subjected the undiluted samples to a series of tests to determine if any conversion to Form I could be observed. Dr. Myerson interpreted Dr. Taylor's data and concluded that Form I was present in some of the test samples.

[14] Teva responded to Merck's opinion evidence with that of Dr. Harry Brittain. Dr. Brittain, in turn, relied, in part, on testing carried out by Dr. James Britten at McMaster University. Dr. Britten's testing partially replicated Dr. Taylor's work but differed in two aspects: he used samples of Form Teva mixed with Teva's excipients and he did not apply heat. Dr. Brittain concluded that Teva's manufacturing process would not convert Form Teva to Form I.

[15] All of the witnesses were well-qualified to speak to the issues bearing on infringement. The determinative issue did not, however, turn on a point of profound intellectual or scientific judgment but rather on a difference of opinion between Dr. Myerson and Dr. Brittain as to the comparative validity of Merck's testing to Teva's manufacturing process.

Claims Construction

[16] I agree with Teva that the 198 Patent is primarily directed at a process for crystallizing efavirenz to make Form I. Efavirenz is identified as a known reverse transcriptase inhibitor. The problem said to be overcome by the Patent was the absence of a reliable method to make Form I. This is described at page 11 in the following way:

> This crystallization process is advantageous over the prior method. The instant method allows one to isolate a crystalline product with consistent physical properties namely the ability to produce the desired crystal form of the product or convert to Form I with mild drying conditions (heating to about 40 to 60°C). The alcohol-water crystallizations have also been shown to reject some impurities carried forward from the chemical synthesis. The final product slurry is less viscous and more homogenous with the instant process and is thus easier to mix and handle.

Claims 1, 2 and 3 of the 198 Patent also claim the compound Form I efavirenz as defined by its disclosed XRPD patterns. Even though the 198 Patent specification is almost entirely devoted to process descriptions, there is nothing inherently objectionable about including claims for a novel compound or compound form produced by the patented process provided that those claims are not otherwise invalid. The inventive promise for Form I efavirenz made by the claimed process is the production of "the desired crystal form" of efavirenz which is said to have "consistent physical properties". It seems to me that the promise of the 198 Patent as read by the skilled reader is only that the Form I crystal is useful. No promise is made that the form is better than any other solid form of efavirenz. Nevertheless, the claims to Form I efavirenz are more than the simple characterization of Form I by XRPD analysis. As I held in *Bristol-Myers Squibb Canada Co. v Mylan Pharmaceuticals ULC,* above, Claims 1 and 2 would be infringed if any detectable amount of Form I is found in Teva's efavirenz product. It does not matter that the amount may be so small that it provides no medicinal advantage.

[17] One other construction issue arises from the evidence. Teva's experts maintain that the person of skill would find an admission in the 198 Patent that Form I efavirenz was publically known. The passages they relied upon for this ostensible admission are the following:

> The synthesis of the reverse transcriptase inhibitor (RTI), (-)-6-chloro-4-cyc1opropylethynyl-4-trifluoromethyl-1,4-dihydro-2H-3,l-benzoxazin-2-one, also known as DMP-266 has been described in US Patent 5,519,021 issued on May 21, 1996 and the corresponding PCT International Patent Application WO 95/20389, which published on August 3, 1995. Additionally, the asymmetric synthesis of an enantiomeric benzoxazinone by a highly enantioselective acetylide addition and cyclization sequence has been described by Thompson, et al., Tetrahedron Letters 1995, 36, 937-940, as well as the PCT publication, WO 96/37457, which published on November 28, 1996.

> The compound was previously crystallized from a heptane-tetrahydrofuran (THF) solvent system. The crystallization procedure required the use of high temperatures (about 90°C) to dissolve the final product. Crystals formed by nucleation during the cooling process. The crystals which were produced were Form II. and are converted to the desired Form I while drying under vacuum at 90°C. This crystallization provided minimal purification and produced material with inconsistent physical properties. The final product slurry was extremely difficult to mix and handle due to its high viscosity and heterogeneous nature.
>
> [See the Applicant's Record at p 16]

[18] Despite the absence of any prior art references expressly disclosing Form I efavirenz the above acknowledgement that Form I "was previously crystallized" is said by the Teva witnesses to be an admission by Merck of public disclosure.

[19] I do not agree that the person of skill would infer a public disclosure from the bare statement that Form I had been previously crystallized. The fact that something has been done says nothing about its notoriety. It is also inconceivable to me that any fair-minded reader of the 198 Patent would interpret the specification in a way that would immediately invalidate all of its compound claims.

Infringement

[20] It is agreed by the parties that Form Teva is a different crystal form of efavirenz than Form I. Accordingly there will be no proven infringement of any of Claims 1, 2 or 3 of the 198 Patent unless Merck can establish on a balance of probabilities that Form Teva converts to detectible levels of Form I during or after the manufacturing process. The mere possibility of infringement is

insufficient: see *Novopharm Ltd v Pfizer Canada Inc*, 2005 FCA 270 at para 24, [2005] FCJ No 1318.

[21] The same issue was before me in the *Bristol-Myers Squibb Canada Co. v Mylan Pharmaceuticals ULC*, above. In that case Merck relied upon an ostensible admission in Mylan's NOA that all known crystal forms of efavirenz will convert to Form I under mild drying conditions. In reliance on what it took to be an admission by Mylan, Merck called no evidence to establish actual conversion. After finding that Mylan's NOA did not admit that its crystal efavirenz product would convert to Form I, I was left with no evidence from Merck to establish its infringement allegation. In the result, I held that Merck had not met its burden.

[22] In holding against Merck on its argument that an adverse inference ought to be drawn from Mylan's failure to either produce its tablets for testing or to conduct its own testing, I made the following points:

> 128 A problem for BMS is that Mylan refused its request for detailed information about its manufacturing processes and provided no information about the final composition of its efavirenz tablet. Mylan also refused to turn over a sample of the final product to allow BMS to conduct its own testing. BMS says that Mylan held all of the evidentiary cards and that an adverse inference ought to be drawn from its failure to disclose that evidence.
>
> 129 There is no doubt that Mylan could have put that issue squarely to rest by producing the information requested by BMS or by producing reliable data from its own testing of the product if any was done. Instead, Mylan asked Dr. Cima to opine about this infringement issue on the strength of his general knowledge of the science of crystallization and the typical manufacturing processes that would be expected for the production of such a tablet. Mylan very deliberately failed to inform Dr. Cima about the details of the process it uses to produce its efavirenz tablet. I agree with BMS that it would have been a relatively simple exercise for Dr. Cima to have

> tested Mylan's efavirenz tablet to determine if Form I was present, but Mylan avoided that option as well.
>
> 130 The essential problem with BMS's position is that it, too, could have done much more to establish the likelihood of conversion. Mylan did not hold all of the evidentiary cards on this critical issue of infringement.
>
> 131 Dr. Myerson admitted that he had the ability and knowledge to make Form [omitted]: see Cross-Examination of Dr. Myerson at p 172.). He also had the ability to subject Form [omitted] to a set of conditions that would mimic a typical wet granulation drying process. I have no doubt that had Dr. Myerson conducted an experiment of this sort and established some level of conversion, BMS would have met its burden of proof - provided that Mylan was unable to contradict it.

[23] There is similarly no basis for drawing an adverse inference in this case. Although Teva refused to turn over samples of Form Teva or its final efavirenz tablets to Merck, Teva acknowledged that Form Teva could be made using a process disclosed in another patent application. In the result, Merck was able to make the compound for testing purposes. Teva also undertook that it would not assert that the sample obtained and tested by Merck was different in character or composition to Form Teva.

[24] I am satisfied that Merck had the capacity to scale up the process and to make a sufficient amount of Form Teva to permit a close, if not exact, replication of Teva's manufacturing process[1]. Instead Merck chose to make a small sample of Form Teva that only allowed it to conduct small scale testing presumably intended to mimic Teva's manufacturing process. The primary dispute among the experts is, then, whether the Merck testing methods are a reliable proxy for what actually

[1] I disagree with BMS's assertion that it was "forced" to make only a small sample. BMS is in the business of making drug compounds and was better equipped than most to make a sample large enough to permit a duplication of the Teva mixing process. This may have been expensive or inconvenient but it was not impossible.

happens during Teva's manufacturing process. Another issue is whether any conversion of Form Teva to Form I actually occurred during that testing.

The Conversion Experiments

[25] The Merck case for conversion is based on a series of tests conducted by Dr. Taylor and interpreted by Dr. Myerson. Because Merck did not have access to the Teva tablets it was required to create the compound in accordance with a disclosed process. Merck had Dr. Taylor synthesize a small quantity of Form Teva which was then subjected to three discrete tests, specifically:

(a) heating Form Teva at [omitted] for 1, 2, 3 and 4 weeks;

(b) grinding Form Teva with mortar and pestle for approximately [omitted];

(c) grinding Form Teva with mortar and pestle for approximately [omitted] followed by hearing at [omitted] for 1, 2, 3 and 4 weeks.

Each of the processed samples was then subjected to an XRPD analysis to determine the presence, if any, of Form I efavirenz.

[26] In addition, Dr. Taylor was asked to synthesize a quantity of Form I by exposing Form Teva to heat at [omitted] for 3.5 and 5.5 days. With this sample, an XRPD analysis of different mixed quantities of Form Teva and Form I was carried out. From this Dr. Myerson was able to plot the intensity ratio versus the ratio by mass of Form I to Form Teva in a given mixture. This, in turn, allowed Dr. Myerson to estimate the percentage of Form I relative to Form Teva in a mixture where the relative weights are not known (see the Myerson Affidavit at para 120, Applicant's Record at p 1336).

[27] Of the three tests carried out by Dr. Taylor only the Form Teva samples that were subjected to grinding followed by heating at [omitted] for several days arguably revealed any Form I. Dr. Myerson asserts at paragraph 127 of his affidavit that XRPD analysis of the Form Teva sample exposed only to mortar and pestle grinding "indicates to me the presence of a very small quantity of Form I efavirenz". This is an unjustified view. I do not accept that the modest and broad XRPD "peak" or "bump" seen in Exhibit K to Dr. Myerson's affidavit is sufficient, on its own, to prove the presence of Form I. Dr. Myerson conceded that reliance on a single XRPD peak would typically be unsound unless it was one of large intensity that did not overlap with that of another compound. Dr. Myerson also acknowledged that the peak observed at the approximate 6.08 position obtained by Dr. Taylor fell within the margin of error for overlap between Forms I and II efavirenz but he refused to fully retreat from the position adopted in his affidavit (see Applicant's Record at pp 5472-5474).

[28] On this point I prefer the evidence of Dr. Brittain who testified that it is the pattern of XRPD peaks that constitutes a fingerprint for a particular crystal structure. According to Dr. Brittain an accurate XRPD identification usually requires an observation of the ten most intense peaks and should not be made on the strength of a single peak (see the Brittain affidavit at paras 33-40, Applicant's Record at pp 3141-3144 and Brittain testimony, Applicant's Record at pp 5961-5962 and p 6028).

[29] Although a small amount of Form I may have been present in these samples, the evidence of its presence was inconclusive at best. It seems to me that the conclusion offered at paragraph 127 of

Dr. Myerson's affidavit and his attempted defence of that position under cross-examination detracts from his overall credibility.

[30] Dr. Taylor also exposed Form Teva to heating at [omitted] for periods of time between 7 to 27 days. These samples, however, had not been subjected to mortar and pestle grinding. Dr. Myerson concedes at paragraph 140 of his affidavit that no measurable Form I could be detected from these heated samples – a finding that he said was consistent with Teva's accelerating aging studies of Form Teva (see paragraph 141, Applicant's Record at p 1339). Nevertheless, Dr. Myerson makes the statement that these results offer evidence of "significantly slower" conversion than samples exposed to grinding (see paragraph 140, Applicant's Record at p 1339). Not surprisingly Dr. Brittain challenged this statement in his affidavit:

> 43. Dr. Taylor also subjected the efavirenz Form [Teva] samples to heating at [omitted] for varying periods up to 28 days. The samples were not subjected to grinding. I have reviewed XRPD patterns at Exhibits "32" to "43" of the Taylor Affidavit, which represent heating at [omitted] for 7 to 27 days, and I do not see evidence for any conversion to Form I. I note that Dr. Myerson comes to a similar conclusion at paragraph 140 of his affidavit, although I disagree with his characterization that conversion to Form I is "significantly slower" absent grinding. Rather, there is simply no evidence of any conversion to Form I. These results, coupled with the grinding-plus-heating experiments discussed below, demonstrate that grinding of pure drug substance was required to induce any conversion of Form [Teva] to Form I.
>
> [Emphasis added] [Applicant's Record at p 3145]

[31] I agree with the above criticism. Dr. Myerson's attempt to interpret a null finding as evidence supporting his theory of conversion is disingenuous and it undermines his credibility. The inference that an objective person would draw from Dr. Taylor's heating experiments is that lengthy

exposure of Form Teva to the maximum temperature used by Teva [omitted] causes no conversion to Form I efavirenz.

[32] Dr. Taylor also exposed Form Teva to heating at [omitted] for several days and observed a conversion to Form I. This outcome is of no relevance to the conversion issue because Teva's manufacturing process does not employ temperatures that high nor does it require prolonged heating. It is not a matter in dispute that Form Teva is less stable than Form I and it will convert if enough heat is applied and the Merck witnesses do not seemingly rely on this result to establish an infringement.

[33] In response to Dr. Taylor's tests, Dr. Britten was asked by Teva to subject a sample of Form Teva and Teva's excipients to mortar and pestle grinding followed by an XRPD analysis. Presumably this approach was designed to illustrate the importance of the excipients to the potential for conversion. Dr. Britten used a highly sensitive XRPD scan which could detect the presence of Form I at levels "better than 1 percent" (see Applicant's Record at p 6109). Perhaps not surprisingly, no Form I was detected. Dr. Britten, however, did not attempt to otherwise replicate Dr. Taylor's work. Dr. Taylor exposed his ground samples to prolonged heating with a view to incubating any Form I "seeds" that were present. It was only through heating that detectible levels of Form I were ultimately found in Dr. Taylor's samples. Dr. Britten did not heat his samples and it was only possible for him to assert that after grinding no amount of Form I was detectable under XRPD analysis.

[34] Given that the sensitivity of Dr. Britten's XRPD analysis was only in the vicinity of 1%, these results do not contradict what Dr. Taylor and Dr. Myerson observed. According to Dr. Myerson's analysis, Dr. Taylor's Form Teva ground samples contained undetectable levels of Form I that only grew to detectable levels after lengthy incubation. It is not possible to say that similar results would not have been obtained had Dr. Britten heated his samples in the same way. Because Dr. Britten failed to match Dr. Taylor's approach, the results Dr. Britten obtained do not clearly establish the significance of the excipient load to the potential for some conversion of Form Teva to Form I from grinding.

[35] I am satisfied that some small amount of Form I was present in Dr. Taylor's samples after grinding because Form I was clearly detected after those samples were heated for several days at [omitted]. This conclusion is not seriously challenged by the Teva witnesses (see the Brittain affidavit at para 43, Applicant's Record at p 3145). The significance of grinding to the conversion of Form Teva is the most plausible explanation for the absence of Form I when Form Teva was simply heated for several days at [omitted]. It was only through the grinding of Form Teva that sufficient energy was introduced to start a conversion to Form I. Once the samples were seeded with Form I the application of heat then enhanced the conversion and produced observable data.

[36] Dr. Myerson estimated the amount of Form I that would be present in Teva's tablets by applying a regression analysis to the data that emerged from prolonged heating of Dr. Taylor's ground samples. According to Dr. Myerson the estimated amount of Form I present in those samples and ostensibly in Teva's tablets was in the range of 0.022% and 0.046%. These amounts

are, of course, too small to be directly detected by XRPD analysis and are predicted only by *ex post facto* extrapolation.

[37] All of these experimental results illustrate the importance of the manual grinding exercise to the conversion findings made by Dr. Myerson. In the absence of grinding or prolonged exposure to temperatures exceeding those used by Teva, Form Teva did not convert.

Conversion By Grinding Form Teva

[38] The central issue in dispute between the parties is whether the mortar and pestle grinding carried out in Dr. Taylor's laboratory is a reliable proxy for the [omitted] that Teva employs in its manufacturing process. The specific issue is whether Teva's process includes the application of sufficient energy to incite a conversion of Form Teva to Form I.

[39] Although Dr. Brittain acknowledged under cross-examination that [omitted] are all capable of causing a phase transformation of a metastable crystal form, he did not concede "that all those processes do the same thing for all compounds" (see the Brittain testimony at p 75, Applicant's Record at p 5975). This is consistent with the evidence of all of the witnesses that the introduction of energy by thermal, mechanical or chemical means may initiate a transformation reaction. According to Dr. Brittain, the issue remains whether the amount of introduced energy is sufficient to overcome the "activation energy barrier".

[40] Teva's manufacturing process is accurately summarized in Merck's Memorandum of Fact and Law at para 40:

[omitted]

[41] It is common ground that Teva's process also involves [omitted].

[42] Dr. Taylor was instructed to grind Form Teva "on its own" and he did not include the Teva excipients in his samples (Applicant's Record at p 5840). Under cross-examination, he said he was not aware of the size of the samples subjected to grinding by his assistant (see Applicant's Record at p 5845). The only quantitative evidence in the record describing the amount of grinding pressure that was applied by Dr. Taylor's assistant is that it was not "light" (see Applicants' Record at p 5844). Dr. Taylor testified that he was not specifically instructed "how exactly to do the grinding" and he could not recall if he was present (see Applicant's Record at p 5839). It appears that Dr. Taylor was not asked to consider the problem of energy equivalency before he proceeded to have his assistant grind the samples without Teva's excipients. As far as I can tell from the record no one involved in setting up the manual grinding exercise considered the materiality of sample size or composition to the outcome of the testing.

[43] Dr. Brittain took issue with Dr. Taylor's failure to include any of the Teva excipients in the sample exposed to grinding. According to Dr. Brittain the presence of excipients in the mixture would be expected to reduce the input energy applied to Form Teva by either [omitted] or grinding. In effect, the dilution of the samples by adding excipients spreads the energy among all of the constituent parts. This point is made at paragraph 23 of the Dr. Brittain's affidavit:

> 23. Even assuming for the moment that the degree of energy used by Dr. Taylor in his grinding experiment would be comparable to that of [omitted], his decision to exclude the excipients in the Teva Tablets from his experiments means that his results cannot be taken

> as being representative of the Teva [omitted] Process, or of the resulting form of efavirenz present in the Teva Tablets. In particular, the Teva Tablets contain [omitted] with the Form [Teva] efavirenz. Accordingly, [omitted] (and other excipients present) would bear the brunt of any [omitted] forces that may be applied to the mixture of ingredients during the manufacturing process. [omitted]. Their presence would greatly reduce the effect of [omitted] conditions experienced by the API. Accordingly, one cannot legitimately rely on the experiments of Dr. Taylor that were performed on unformulated efavirenz Form [Teva] to deduce whether there would be any amount of phase conversion during the Teva Granulating Process.
>
> [Footnotes omitted] [Applicant's Record at p 3138]

[44] Dr. Brittain also challenged Dr. Myerson's equation of hand grinding by mortar and pestle with [omitted] used in Teva's tabletting process. According to Dr. Brittain, it is well-known that mechanical grinding applied to a compound can induce a phase transformation. The differences in the two approaches are described by Dr. Brittain at paragraphs 27 and 28 of his affidavit:

> 27. While [omitted] pressure (or stress) on the mixture, it does not equal (or even come close to) the pressure that results from grinding in a mortar and pestle. There are also significant differences between the two in terms of the way they apply force. These differences are clear when one considers that [omitted]. In contrast, when Dr. Taylor used a mortar and pestle, he was in effect putting Form [Teva] efavirenz between a rock and a hard place for [omitted]. The result is that Dr. Taylor's grinding experiments almost certainly exerted far more stress and pressure on the API than would occur in [omitted]. This is particularly evident given that Dr. Taylor did not include any of the excipients during his grinding work.
>
> 28. I also note that Dr. Taylor provides no information regarding the degree of pressure that was exerted during his grinding experiments. Exhibit "44" of the Taylor Affidavit merely states that a sample was "ground for 11 minutes with a mortar and pestle". Was this a heavy grind, or a light grind? It is difficult to replicate Dr. Taylor's experiments without more information on how heavy of a grind was used. There was no attempt by Dr. Taylor to determine what amount of pressure had to be applied, or for how long, in order to mimic the force that would be applied by a [omitted]. As noted

> above, [omitted] the Teva [omitted] Process. Nevertheless, Dr. Taylor simply ground his samples for the same amount of time as the material is mixed in the Teva [omitted] Process.
>
> [Applicant's Record at p 3140]

It is noteworthy that under cross-examination Dr. Brittain was not challenged on these points.

[45] Given the importance of the grinding step in seeding the samples with Form I, the failure by Dr. Myerson and Dr. Taylor to establish any apparent standards or to otherwise control for the energy that was applied during Dr. Taylor's conversion grinding experiments is a surprising deficiency. Dr. Myerson's experience-based opinion was only that the two processes would exert "roughly equivalent" levels of energy. In the absence of any empirical evidence of energy equivalency, considering the minute quantities of Form I extrapolated by Dr. Myerson to be present after grinding and in the face of Dr. Brittain's evidence, I am not prepared to infer that the uncontrolled use of mortar and pestle grinding of a small undiluted sample for [omitted] is a reliable surrogate for the [omitted] used by Teva. Indeed, the inference I draw from the essentially uncontradicted evidence of Dr. Brittain is that the process followed by Dr. Taylor would apply levels of energy to Form Teva far in excess of what would be expected from Teva's manufacturing process. Although minute and undetectable quantities of Form I were likely present in Dr. Taylor's mortar and pestle samples, I am not satisfied that the same can be said for the Teva tablets. Of course, if I am wrong about that Merck always has the option of commencing an infringement action once those tablets reach the market.

[46] In the result, Merck has failed to meet its burden of proving that Teva tablets will contain Form I efavirenz and its application is dismissed.

[47] The issue of costs is reserved pending the receipt of written submissions from the parties not to exceed 10 pages in length. Teva will have 21 days to make its submissions and Merck will have 14 days to respond.

JUDGMENT

THIS COURT'S JUDGMENT is that this application is dismissed.

THIS COURT'S FURTHER JUDGMENT is that the issue of costs is reserved pending the receipt of written submissions from the parties not to exceed 10 pages in length. Teva will have 21 days to make its submissions and Merck will have 14 days to respond.

"R.L. Barnes"

Judge

FEDERAL COURT

SOLICITORS OF RECORD

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