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Case Comment

BORTEZOMIB BATTLES: A TALE OF LICENSEES AND BURDENS

Millennium Pharmaceuticals, Inc v Zyfas Medical Co [2023] SGHC 360

[2024] SAL Prac 16

Exclusive licensees of patents enjoy a certain amount of protection. The High Court was recently given an opportunity to throw some light on who an exclusive licensee is. The High Court also considered the circumstances under which a claimant may reverse the burden of proving infringement of a patented process.

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I. Introduction

1 Bortezomib is an international non-proprietary name for a drug used for treating multiple myeloma and mantle cell lymphoma – two forms of blood cancer. It was developed in the 1990s and has been approved for medical use since the early 2000s. The active chemical compound of bortezomib has no product patent protection in Singapore, and drugs incorporating bortezomib may be sold without fear of patent infringement.

2 There are many ways to synthesize bortezomib. One such method involves making a boronic ester by using zinc chloride as a catalyst as part of a Matteson homologation protocol, which was patented in Singapore in 2012 ("2012 patent") by Millennium Pharmaceuticals ("MP"). In 2018, MP was granted another

patent ("2018 patent") for a method allowing for large scale manufacture of bortezomib. A bortezomib drug was distributed by Johnson & Johnson ("J&J") in Singapore as "Velcade".

3 A Singapore partnership, Zyfas Medical Co, applied to the Health Sciences Authority ("HSA") for approval to import, market and distribute in Singapore a generic version of bortezomib made by Dr Reddy's Laboratories Ltd ("DRL") as "Myborte". The application identified the active ingredient as bortezomib and was approved by the HSA in 2019. MP commenced a suit against Zyfas for infringing its 2012 and 2018 patents. J&J joined the suit against Zyfas subsequently.

4 MP also filed a separate application to court under reg 23(2) of the Health Products (Therapeutic Products) Regulations 2016, seeking a declaration that Zyfas' application contained a false or misleading declaration in a material particular or omitted to disclose a matter that is material to the application for registration of a therapeutic product. Dedar Singh Gill J's decision[1] to grant the declaration was upheld by the Court of Appeal.[2] Essentially, the Court of Appeal held that Zyfas should have declared the existence of MP's patents and that the acts permitted by the registration would not infringe MP's patents.[3]

5 MP's infringement suit against Zyfas finally came before Gill J[4] who held that the 2018 patent was invalid and that MP failed to establish infringement of the 2012 patent by the manufacture of the generic bortezomib distributed by Zyfas. In coming to his decision, besides impressively grappling with the scientific intricacies of the associated biochemistry, Gill J had to consider a few interesting issues, including:

(a) whether J&J had standing in the infringement suit; and

1 *Millennium Pharmaceuticals, Inc v Zyfas Medical Co* [2020] SGHC 28.
2 *Zyfas Medical Co v Millennium Pharmaceuticals, Inc* [2020] 2 SLR 1044.
3 *Zyfas Medical Co v Millennium Pharmaceuticals, Inc* [2020] 2 SLR 1044 at [42].
4 *Millennium Pharmaceuticals, Inc v Zyfas Medical Co* [2023] SGHC 360.

(b) whether s 68(1) of the Patents Act[5] could be invoked to shift the burden of proof of infringement to Zyfas.

II. Standing of an exclusive licensee

6 Section 74(1) of the Patents Act[6] provides as follows:

> The holder of an exclusive licence under a patent *shall have* the same right as the proprietor of the patent to bring proceedings in respect of any infringement of the patent committed after the date of the licence; and references to the proprietor of the patent in this Act relating to infringement *shall* be construed accordingly. [emphasis added]

7 Infringement proceedings brought by an exclusive licensee has the benefit of losses suffered (or likely to be suffered) by the exclusive licensee being taken into consideration when relief is granted.[7]

8 J&J claimed to be an exclusive licensee within the meaning of s 74(1) because it was an exclusive distributor of bortezomib produced under the patented processes of the 2012 and 2018 patents. Section 2(1) of the Patents Act defines an exclusive licence as "a licence from the proprietor of … a patent conferring on the licensee … any right in respect of the invention to which the patent … relates".

9 J&J submitted that the term, "any right", encompasses the right of distribution of a product of a patented process.

10 J&J alleged that it distributed bortezomib produced under the patented processes by an affiliated company, Janssen Products LP ("Janssen"), under an exclusive licence conferred by MP. J&J claimed to be the only distributor of bortezomib

5 Cap 221, 2005 Rev Ed.

6 The current version of s 74(1) in the Patents Act 1994 (2020 Rev Ed) states:

> The holder of an exclusive licence under a patent *has* the same right as the proprietor of the patent to bring proceedings in respect of any infringement of the patent committed after the date of the licence; and references to the proprietor of the patent in this Act relating to infringement *are to* be construed accordingly. [emphasis added]

7 Patents Act (Cap 221, 2005 Rev Ed) s 74(2).

in Singapore. These claims were unsurprisingly challenged by Zyfas. Unfortunately for J&J, its key witness admitted under cross-examination that J&J was not the exclusive licensee.

11 Gill J noted that there was no documentary evidence of J&J's exclusive dealings.[8] Although J&J had tendered evidence that it was the registrant of an active product registration for "Velcade" with HSA from 2005, it did not show that J&J was a distributor, much less an exclusive licensee.

12 Gill J also took clear note that neither the highly relevant exclusive licence agreement between MP and J&J's affiliated company nor the distributorship agreement between J&J and its affiliated company were produced. Even if s 2(1) of the Patents Act was susceptible to the broad interpretation that an exclusive distributor constitutes a statutory exclusive licensee, there was no evidence to prove the nature of the rights held by J&J's affiliated company being rights which it could have granted to J&J.[9]

13 As such, Gill J concluded that J&J failed to show that it was an exclusive licensee, and that even if infringement were made out, J&J cannot be awarded damages or an account of profits.[10]

14 The following observations may be made in light of the above:

(a) A HSA product registration *per se* may not be sufficient for establishing distributorship or licensee status.

(b) In order to establish standing as an exclusive licensee, it is important to produce relevant evidence such as an exclusive licence agreement as pointed out by the court.

(c) It remains an open question whether s 2(1) provides a broad interpretation of "exclusive licensee" in

8 *Millennium Pharmaceuticals, Inc v Zyfas Medical Co* [2023] SGHC 360 at [121].
9 *Millennium Pharmaceuticals, Inc v Zyfas Medical Co* [2023] SGHC 360 at [119].
10 *Millennium Pharmaceuticals, Inc v Zyfas Medical Co* [2023] SGHC 360 at [122].

the sense that distributor rights qualify as "any right in respect of the invention".

(d) In order to establish exclusive distributor rights in the context of the standing of an exclusive licensee, it is important to produce relevant evidence, for example, an exclusive distributorship agreement.

(e) Even if exclusive distributor rights are established, it may be prudent to establish that the nature and content of the rights held are consistent with that of an exclusive licence.

(f) It appears that the court may entertain the possibility of an exclusive licensee deriving its rights indirectly from the patentee via the intermediation of another party.

III. Shifting of burden

15 It is well established that the party claiming patent infringement bears the burden of proving the claim. This is the case whether the patent relates to a product or process. Products are sold through trade channels which a patentee may follow to obtain a sample for analysis. Processes, by comparison, may be performed within secured industrial closed doors and are not as readily accessed for analysis. Of course, what happens behind closed doors may not necessarily be infringing processes. Section 68(1) of the Patents Act 1994[11] attempts to balance these concerns by providing that:

> In any proceedings for the infringement of a patent, where the subject matter of the patent is a process for obtaining a new product, the burden of proving that a product is not made by the process is on the alleged infringer if the product is new or a *substantial likelihood* exists that the product is made by the process and the proprietor of the patent has been unable through reasonable efforts to determine the process actually used. [emphasis added]

11 2020 Rev Ed.

16 When successfully activated, the burden of proof is reversed such that the alleged infringer must then prove that a product is not made by the patented process in question. As a safeguard, the court should not unreasonably require the disclosure of any manufacturing or commercial secret when considering whether the burden of proof imposed by s 68 is discharged.[12]

17 MP and J&J argued that the burden of proof should be shifted to Zyfas when considering infringement of the relevant process claims of the 2012 patent. An essential element of its claim 1 (upon which other relevant claims depended) dictated the use of an ether solvent of low miscibility[13] with water (such as methyl tert-butyl ether or MTBE), that is, an ether solvent that does not mix well with water. MP contended that the purity of the bortezomib achieved by DRL indicates that an ether solvent of low miscibility with water must have been used. Asserting that it was unable through reasonable efforts to determine the actual process used by DRL to manufacture bortezomib, MP moved to invoke s 68 to shift the burden to Zyfas to prove that DRL's process did not infringe the 2012 patent.

18 Zyfas contended that DRL's process did not use water-immiscible ether solvents to manufacture bortezomib, pointing out that there were other known ways outside of the 2012 patent to manufacture bortezomib. Despite MP's attempts to scientifically discredit DRL's process description of manufacturing bortezomib, MP failed to convince the court that DRL's process could not have yielded the bortezomib purity achieved or that the only way to achieve such purity was through the patent process. The court thus did not find the existence of a "substantial likelihood" that Zyfas' generic bortezomib was manufactured by the patented process.

19 Notably, Zyfas had also invited MP and J&J in July 2019, early 2020 and April 2021 for site visits at DRL's facilities in

12 Patents Act 1994 (2020 Rev Ed) s 68(2).

13 "Miscible" refers specifically to "capable of mixing in any ratio without separation of two phases": see Merriam-Webster Dictionary, "miscible" <https://www.merriam-webster.com/dictionary/miscible> (accessed 10 July 2024).

Telangana, India, to inspect DRL's process of manufacturing bortezomib. MP's affiliated company, Janssen, had an office and technical staff in India. MP and J&J declined all invitations, citing the COVID-19 situation which Gill J found to be a pretext for refusing to visit. Gill J observed that:[14]

> … even if there had indeed been a lockdown between 12 May and 19 June 2021 … the plaintiffs could very well have conducted a site visit after the lockdown had ended. There was a significant amount of time prior to the commencement of trial in October 2021 for the plaintiffs to have conducted their own investigation on the process adopted by DRL … The plaintiffs could have either sent their employees in India to undertake the site visit or hired external third-party experts to do so.

20 The court went on to dismiss the case on infringement entirely.

21 It may be readily seen from this case that the court does not take the shifting of the claimant's conventional burden of proof lightly. A claimant seeking to invoke a reversal of burden of proof must therefore undertake sufficient homework to:

(a) establish the existence of a substantial likelihood that the patented process was used in manufacturing a product (unless the product is new); and

(b) demonstrate that reasonable efforts have indeed been made to determine that the process was actually used by an alleged infringer.

22 Declining an invitation (especially multiple invitations) for inspection of the process used is probably a decision that should only be made very cautiously.

14 *Millennium Pharmaceuticals, Inc v Zyfas Medical Co* [2023] SGHC 360 at [271].