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INFRINGEMENT ON NEW-USE PATENTS – REASONABLY REQUIRED EFFECTIVE MEASURES

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1. INTRODUCTION

In 2017 an article appeared by Kleemans and Drok about the interpretation of Swiss-type claims and EPC-2000 claims[1]. In this article, they discuss the question of how infringement on a second medical use patent has to be assessed and if it should matter whether the claims were written in the Swiss-type format or the EPC-2000 format. The Dutch Supreme Court in The Hague in the MSD/Teva[2] verdict of November 2017 judged that according to the Dutch patent law it does not matter. A year later the highest English judge, the UK Supreme Court ("UKSC"), judged in the Lyrica® case that in English patent law it most definitely is relevant for the assessment of infringement in what format the claims were written[3]. The Dutch Supreme Court further explained in MSD/Teva how the infringement on a "new-use patent"[4] has to be assessed in Dutch patent law.

We will discuss the approach of the Dutch Supreme Court in this article. We will especially focus on the questions that coincide with the requirement of the Supreme Court that producers or sellers of generic medications[5] have to take "effective measures that can be reasonably required of them" to prevent that their product will be dispatched for the patented new use. What are effective measures? Does it matter in this case what kind of new-use patent it concerns? Does the generic have to inform the patentee of the measures that they are taking? These are questions that are potentially very significant in practice. The MSD/Teva verdict does not provide much support for the answers to these questions. Other case law of the lower courts also does not (yet) provide support.

After this, we will first discuss what we understand as a "new-use patent"[6]. Next, we will dive into the MSD/Teva verdict and provide it with commentary. We will concentrate on the requirement of the reasonably required effective measures. Then, we will address the question of which measures can be effective in practice and if such measures can reasonably be required of the generic.

2. NEW-USE PATENTS

The European Patent Convention and the Dutch Patent Act enable people to obtain a patent directed to a new use of an already known compound[7]. The most well-known example of this the "classic" second medical indication. In the prior art, a compound is known of which it is also already known that they can be used for a certain disease (a.k.a "indication"). If somebody then discovers that this known compound can also be used for a different disease, this person may in principle obtain a patent for this[8]. Such a patent is referred to as a second medical indication patent. Further discoveries of third,

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1 R.M. Kleemans & J.D. Drok, "Interpretatie van Swiss-type claims en EPC 2000 claims", *IER* 2017/3, afl. 1, p. 9-21.

2 HR 3 November 2017, ECLI:NL:HR:2017:2807, *NJ* 2018/178 (*MSD/Teva*).

3 Supreme Court of the United Kingdom 14 November 2018, *Warner-Lambert Company LLC v. Generics (UK) Ltd t/a Mylan and another* [2018] UKSC 56.

4 We will explain this term in paragraph 2.

5 For simplicity reasons hereafter the producer or seller of a generic medication "the generic". When talking about a generic medication we in principle also mean the so-called *biosimilar*.

6 To perhaps be more precise: new medical use-patent, since the use in the patents we are referring to our still medical uses.

7 See for example the article by Kleemans and Drok, paragraph 2.

8 Of course assuming that such a use is new and inventive.

fourth (and so on) indication may also in principle be patentable. Initially, the claims of such a second (or further) medical indication patent needed to be written in the Swiss-type format[9]. After the new European Patent Convention in 2000 ("EPC 2000") entered into force, it is possible to write a claim in the EPC-2000 format[10].

The possibility to obtain a patent on a new use of a known compound is not limited to the second (or further) medical indication. This follows from a decision of the Enlarged Board of Appeal of the European Patent Office (EPO) in the case G2/08[11]. In said case, the Enlarged Board of Appeal answered three questions. The first question addressed whether the European Patent Convention allows that a patent is granted in the situation in which it is already known that a disease can be treated with a certain medication, and that the invention is that in an advantageous way, the same medication is used for the same disease, but using a different treatment. The second question builds on the first question and addresses whether a new dosage regime is patentable. The third question concerns whether the so-called Swiss-type format is no longer allowed since the EPC 200 entry into force. The Enlarged Board of Appeal answered the last question by stating that the Swiss-type format is no longer allowed after the entry into force of the EPC 2000. This decision at that point in time did not have retroactive effect. Because of this, for around 10 years it was possible to have a patent with both Swiss-type and EPC-2000 claims.

Back to the first two questions. The Enlarged Board of Appeal decoded that the EPC allows that a patent is granted for a different treatment of a disease using a compound that was already used for said disease in the prior art. Furthermore, the Enlarged Board of Appeal also decided that in principle a patent can be granted for any new dosage regime of a medication for use in a disease, wherein the use of that medication was already known in the prior art. The Enlarged Board of Appeal came to this decision, because they are of the opinion that art. 54(5) EPC has to be interpreted broadly. The Enlarged Board of Appeal found support for this position in, amongst other things, the English version of this article, where they use the phrasing "*any specific use*"[12]. The Enlarged Board of Appeal was of the opinion that this specific use was not limited to the classic second (or further) medical indication. Naturally, patents granted for such a specific use do need to comply with (amongst other things) the requirements for novelty and inventive step. The Enlarged Board of Appeal has given some directions for this in G2/08.

As a consequence of G2/08 the possibility to obtain a patent for a new use is no longer limited to a classic second (or further) indication. In principle, it is possible to obtain a patent for any new use of a known compound, as long as it meets the general requirements for patentability. Here is a few examples of the possibilities. It is possible to patent so-called dosage regimes. A dosage regime concerns the amount and/or frequency of administration of a certain compound for a certain disease, where the use of the compound for this disease was already known from the prior art[13]. Patenting the route or way of administration is another possibility. Let us assume that it is known from the prior art to administer a compound for a certain disease (e.g.) intravenously (IV). If somebody discovers that it is possible to administer that same compound for treating the same disease by administering subcutaneously (under the skin), a patent may be granted for this route of administration. It could for instance be surprising that a

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9 In short: *"Use of [substance X] in the manufacture of a medicament for the treatment of [disease Y]"*.

10 In short: *"[Substance X] for use in the treatment of [disease Y]"*.

11 Enlarged Board of Appeal of the European Patent Office 19 February 2010, ECLI:EP:BA:2010:G000208.20100219, G0002/08 (*Dosage regime/Abbott Respiratory*).

12 In the Dutch translation of the article the phrasing "*a specific use*" is used, which we believe is rather unfortunate since the French translation also speaks of "*Toute utilisation spécifique*".

13 In the EPC-2000 format a dosage regime claim can be written as follows: *"[Substance X] for use in the treatment of [disease Y], whereby [X] is administered by dosage regiment [Z]"*.

subcutaneous administration is possible or that an advantageous effect is achieved through subcutaneous administration. Imagine that the treatment of a certain disease with a certain compound is known from the prior art. It could be a patentable invention that a specific group of patients in particular responds in an especially beneficial way to the compound (even if this group is part of a bigger group of patients already being treated with this compound in the prior art).

In practice, there have been instances that the invention is a combination of different forms of a new use. The patent claim could for instance be directed towards a treatment according to a certain dosage regime, wherein the compound is administered in a certain way. The MSD/Teva case concerned a new-use patent wherein the claims (in Swiss-type format) were aimed at the use of ribavirin in the treatment of a specific patient group according to a specific dosage regime[14].

Due to the many possibilities to obtain a patent for a new use of a compound, in this article we will use the term "new-use patent". We have elaborated extensively on the different types of new-use patents, because it could be relevant in the question of infringement what type of new-use patent the proceedings are about.

3. THE DUTCH SUPREME COURT IN MSD/TEVA

The verdict of the Supreme Court in the MSD/Teva case has already led to a lot of comments[15]. The Supreme Court has answered several questions in this case that had already been addressed in the lower courts. However, the verdict has also left some questions, which are very important in practice, unanswered. In order to fully understand this case, it is helpful to briefly discuss the relevant facts.

MSD is the holder of European patent 0 956 861 (EP '861)[16]. This patent, briefly put, concerns a dosage regime for the use of ribavirin and interferon-α in the treatment of a subgroup of patients with the hepatitis C virus (HCV). So, a combination of a dosage regime and a subgroup indication. Claim 1 is in the Swiss-type format and reads:

> *"The use of ribavirin for the manufacture of a pharmaceutical composition for treating a patient having chronic Hepatitis C infection to eradicate detectable HCV-RNA wherein the pharmaceutical composition is for administering an effective amount of ribavirin in association with an effective amount of interferon alpha, characterised in that the ribavirin in association with the interferon alpha is for administration for a time period of 40-50 weeks, the patient is an antiviral treatment naïve patient, and the patient is one having a HCV genotype 1 infection and a viral load of greater than 2 million copies per ml of serum as measured by HCV-RNA quantitative PCR."*

On the priority date of EP '861 the compound ribavirin was already known. Actually, the prior art goes even further: the use of ribavirin and interferon-α in the treatment of HCV was also already known. This can be concluded from EP 0 707 855, which is prior art for EP '861. EP 0 707 855 discloses a combination of ribavirin and interferon-α for the treatment of (amongst others) hepatitis C patients that did not receive treatment before ("naïve patients") for the duration of 6 to 12 months. This patent does not discern between the genotypes of the hepatitis C virus. EP '861 thus differs from the prior art in the choice made for a particular type of patient and a limitation on the dosage regime[17].

[14] The Dutch Court of Appeal in The Hague has named said claim, not completely accurately, a "subgroup indication".

[15] See for instance the following annotations: Ch. Gielen in *NJ* 2018/178, L.E. Dijkman in *BIE* 2017/6 en Schutjens in *JGR* 2017/34.

[16] Initially Schering Corporation was the patentee.

[17] See also the verdict of the Dutch Appeal Court The Hague of 14 July 2015, ECLI:NL:GHDHA:2015:1899, rov. 4.1.

Opposition was filed against the grant of EP '861. The Technical Board of Appeal of the European Patent Office has maintained the patent, at two separate occasions, in its original form[18]. Teva markets generic ribavirin tablets in the Netherlands. The Summary of Product Characteristics ("SmPC") of these tablets contains a so-called "carve-out", where the ribavirin indication that falls within the scope of EP '861 is not mentioned. Normally, the SmPC of a generic medication has to be essentially identical to that of the reference medication. Article 11 of the Directive 2001/83/EC relating to medicinal products for human use, provides an exception in case a certain indication or dosage form of said medication still falls within the scope of the patent rights of a third party. In that case a reference to said indication or dosage form may be omitted in certain parts of the SmPC. This is what people refer to as a *skinny label*. MSD[19] claims that Teva infringes EP '861 in the Netherlands by selling ribavirin tablets. They started main proceedings against Teva, in which they demanded an injunction against infringement amongst other things. Initially, MSD was unsuccessful: the Court in The Hague and the Court of Appeal in The Hague both rejected the injunction. In the assessment of the case, the Court of Appeal discerned between the different type of new-use inventions for which a patent may be obtained. The Court of Appeal admitted that there are different instances of a new use for which a patent can be obtained. The Court of Appeal discerned two such cases in consideration 4.2:

- The compound is used in a different disease than the disease in which it was used in the prior art, the classic second medical indication (the Court of Appeal called it: 2M-I);
- The compound – like in EP ;861 – is used on a subgroup of the group in which the known indication was used, the subgroup indication (the Court of Appeal called it: SG-I).

According to the Court of Appeal there is a significant difference between these two categories of inventions, and that difference would have consequences for the scope of protection (among which, according to the Court of Appeal, the acts concerned). The Court of Appeal explains this in considerations 4.3 – 4.5 and comes to the conclusion that their verdict in the Novartis/Sun[20] was not applicable on the so-called SG-I patents. The Court of Appeal then first assessed the question of whether Teva directly infringed EP '861. According to the Court of Appeal, it is at least required that the person skilled in the art would understand from the SmPC/package insert of Teva's generic product that Teva's product is specifically for use with the subgroup mentioned in the patent's claim. That is not the case, according to the Court of Appeal because of (simply said) the *carve-out* of the indication according to EP '861 from the SmPC/package insert of the Teva product (considerations 5.1 – 5.5). the Court of Appeal then rejects indirect infringement in considerations 6.1 – 6.5. According to the Court of Appeal, ribavirin is not a "wezenlijk bestanddeel van de uitvinding" (essential component of the invention) within the meaning of art. 73 of the Dutch Patent Act.

The Dutch Supreme Court disagrees on all points with the verdict of the Court of Appeal. All complaints MSD has aimed at those verdicts, succeed according to the Supreme Court. Firstly, the Supreme Court judges that by making a distinction between 2M-I and SG-I patents, the scope of protection of EP '861 (an SG-1 patent) has in general been laid down. According to the Supreme Court, the Court of Appeal has categorically given a more limited scope of protection to SG-I patent, or at least categorically given a different criterion for the scope of protection (consideration 3.3.1). The Supreme Court then addresses the scope of protection of Swiss-type claims. We prefer, as indicated before, the term new-use patent, but in this instance we will follow the terminology used by the Supreme Court.

[18] T1399/04 and T1545/98.

[19] In first instance still Schering Corporation.

[20] Court of Appeal The Hague 27 January 2015. ECLI:NL:GHDHA:2015:1769 (*Novartis/Sun*). Sun instituted cassation. The Supreme Court confirmed the verdict in HR 14 April 2017, ECLI:NL:HR:2017:692 (*Sun/Novartis*).

The Supreme Court points out that a patent with Swiss-type claims ("a Swiss-type patent") carries with it a difficulty that mainly presents itself when there is an application of the medication for which there is no valid patent right (anymore). The Supreme Court refers to the situation in which the patent concerning the first medical indication has expired. The use of a medication for a "patent free indication" should not be, as understandably judged by the Supreme Court, blocked by the patentee of a new-use patent. Thus, the Supreme Court has provided the following rules to judge the direct infringement on a Swiss-type patent (consideration 3.4.4, translated into English):

This is why it has to be assumed that a producer or seller only directly infringes a patent with Swiss-type claims when they foresee or should foresee that the generic product that they produce or offer will consciously be used for the treatment which the second medical indication patent concerns. For this it is required that the person skilled in the art based on the SmPC and/or the package insert, or through any other circumstances, will conclude that the product is (also) used or suitable for said treatment. The producer or seller will then have to take all reasonably required effective measures to prevent that his product will be distributed for the patented second medical indication. The mere presence – as in the current case – of a carve-out in the sMPC and package insert of the generic medicament is in general not sufficient to exclude the presence of direct infringement (HR 14 April 2017, ECLI:NL:HR:2017:692, NJ 2017/296, rov. 3.5.2).

A distinction in the type of patent is in this case not allowed. It is required but also sufficient, according to the Supreme Court, in all cases of (direct) infringement on Swiss-type patents that (i) the person skilled in the art will concluded that the generic product is (also) intended or suitable for the treatment disclosed in the Swiss-type patent, (ii) the generic foresees or should foresee that the generic product will consciously be used for said treatment, and (ii) they do not take the measures discussed in considerations 3.4.4 (consideration 3.5).

Concerning indirect infringement, the Supreme Court considers in consideration 3.6 that it is irrelevant for the assessment of the infringement question whether the claims are written as Swiss-type claims or as EPC-2000 claims. Indirect infringement on a patent with Swiss-type claims in the Netherlands is thus possible. In consideration 3.6.4 the Supreme Court judges that a producer of a generic medicament indirectly infringes on a Swiss-type patent when they offer or deliver said medicament to people that are not allowed to use the invention, and that they know, or should know given the circumstances, that said medicament is suitable and is intended for the patented new indication. According to the Supreme Court, it is not an objection that a generic could infringe both directly and indirectly a Swiss-type patent in this way. The verdict finally contains an interesting explanation of the phrase "essential component of the invention" in consideration 3.6.6. We will not discuss this further in this article.

4. COMMENTARY

The MSD/Teva verdict creates clarity in a lot of important aspects concerning the infringement of a new-use patent. However, the verdict also leaves some questions unanswered. It concerns several matters that, in our opinion, could be very relevant in practice. We will now discuss some of these matters.

Swiss-type vs. EPC-2000 claims

In MSD/Teva the Supreme Court consistently speaks of Swiss-type claims. In the considerations that are most relevant to us (considerations 3.4.4, 3.5, 3.6.3 and 3.6.4) they discuss the rules for infringing on a new-use patent with such claims. It is our opinion that said rules also apply to a new-use patent with EPC-2000 claims, at least where it concerns the reasonably required effective measures. It appears from consideration 3.6.3 of MSD/Teva that the Supreme Court considers the scope of protection of Swiss-type claims and EPC-2000 claims equal. In our opinion, there is no reason to discern between the two types of claims in the question of what the reasonably required effective measures to take are. The reason why the Supreme Court only speaks of Swiss-type claims in MSD/Teva is most likely due to the fact that EP '861 (solely) contains Swiss-type claims.

The criteria for infringement

In MSD/Teva the Supreme Court provides two criteria for the assessment of direct infringement:

a) The generic foresees or should foresee that the generic product will consciously be used for the treatment covered by the new-use patent ("the patented treatment"). This requires that the person skilled in the art based on the SmPC, the package insert and/or other circumstances would conclude that the medicament is (also) intended for the patented treatment. We call this the foreseeability-requirement.
b) If the foreseeability-requirement is met, there is a second criterion ("the effective measures requirement"). The generic has to take all the required effective measurements to prevent that the generic product is distributed for the patented indication. Wat such measures could be has not been specified by the Supreme Court. They only judge that in general a carve-out is not sufficient[21].

We are of the opinion that the first criterion, the foreseeability-requirement, is easily met in practice. Several reasons can be mentioned in support of this. It can be assumed that the person skilled in the art[22] is aware that the reference medicament (usually the medicament of the patentee) is used for several indications. Thus, he knows that the generic medicament is (also) suitable for the patented indication. In the situation that the SmPC does not contain a carve-out of the patented indication, it is evident that the person skilled in the art will conclude that the medicament is (also) intended for said indication. However, if the SmPC does contain a carve-out, this does not necessarily change the situation. It has to be considered that the indication cannot completely be carved out of the SmPC. The carve-out is only possible under certain headings of the SmpC, in particular heading 4.1 (therapeutic indications) and heading 4.2 (posology and method of administration). Regulatory-wise it is not possible to remove references to the patented indication from other parts of the SmPC. See for instance the factual finding (ix) from the MSD/Teva verdict. The Supreme Court has determined amongst other things in said finding that heading 5.1 of the SmPC of Teva's ribavirin describes a clinical study in which the medicament has been used according to the patented indication. The person skilled in the art will, despite the carve-out, find a pointer in this that that medicament is (also) intended for the patented indication.

More importantly, the person skilled in the art is familiar with the practice of the issuing of medications. He is aware that health insurance companies instruct pharmacists to issue a medicament as cheaply as possible. Since the generic medication contains the exact same active ingredient as the reference medicament, it can be assumed that health insurance companies will prefer that the generic medicament (seeing as this is most likely cheaper than the reference medicament) is prescribed for as many patients as possible for all indications[23]. This is reinforced by the fact that in the Netherlands, doctors prescribe based on the active ingredient, without mentioning the indication for which the medicament is prescribed. The pharmacist in most

[21] The UKSC clearly has other thoughts on this last point. In the English patent law a carve-out is in principle sufficient, according to the UKSC in the Lyrica® case. Although it is shocking to read in the Lyrica® verdict of the UKSC that the Ductch judge would have come to the same verdict in this matter as the English judge (consideration 152). The UKSCS was apparently not aware of the MSD/Teva verdict, or has misunderstood this verdict.

[22] Gielen in his NJ-noot and Dijkman in his BIE-noot correctly, in our opinion, point out that it is curious that the Supreme Court here refers tot he person skilled in the art and not the producer or seller.

[23] In the case of a biosimilar this might be different. Since such a product is made from biological materials, a biosimilar will not be identical to the reference product. There is a certain reluctance observed among doctors to switch patients who are being treated with the reference product to a biosimilar.

cases will thus be unaware for what indication (a "free indication" or a "patented indication") they are issuing the medicament.

In paragraph 5 we will discuss the second criterion, the effective measures requirement, further. However, we would already like to point out that this criterion will only become relevant once the first criterion has been met. Only then a carve-out will in general be considered as insufficient.

It is interesting to further explore what the Supreme Court finds with regard to the indirect infringement of a new-use patent. In consideration 3.6.3 the Supreme Court states that, for indirect infringement, a patent with Swiss-type claims is essentially equal to a patent with EPC-2000 claims. Both types of patents can be indirectly infringed under Dutch patent law. This is the case if the generic *offers or supplies the medicament to people that are not allowed to use the invention and given the circumstances he should now that the medication is suitable and will be used for the patented second medical indication.* This seems like a less stringent infringement-requirement than the one for direct infringement. The Supreme Court states, in not so many words, that the generic can escape infringement by complying with the effective measures requirement. As we explained before when discussing the foreseeability requirement, it is to be expected that the judge will assume fairly quickly that the medicament is suitable and intended for the patented indication. It is obvious that it is suitable for said indication. The generic product contains the same compound as the reference product and is therefore by definition suitable for the same use as the reference product. The generic is also aware of this: the regulatory admission of the generic compound is after all largely based on the dossier of the reference compound. It also seems that it can quickly be assumed that the generic compound (at the least also) will be intended for the patented indication. It is likely that the generic medicament will be supplied for this indication, at least incidentally[24]. In this way, indirect infringement is easily established. However, we believe that it is unlikely that the Supreme Court intended to establish a criterion for indirect infringement which is less stringent than the criterion for direct infringement. Therefore, we believe that the generic can escape indirect infringement of a new-use patent if they take all reasonably required measures to prevent that the generic product is issued for the patented indication (in other words: meets the effective measures requirement). If that is the case, they can in our opinion successfully defend himself against a claim based on indirect infringement.

Burden of proof

An important question is that of the distribution of the burden of proof: which party has the burden of proof for which points, and therefore also the risk of proof. We don't see any very clear pointers for this in the MSD/Teva verdict. The starting point for the question about the burden of proof is Article 150 of the Code of Civil Procedure. In a "normal" infringement procedure, it will be the patentee who makes claims that the generic product infringes his patent[25]. The patentee will have to state, and in the event of a dispute prove, that the product of the generic is infringing. We conclude from this that in a normal infringement procedure the patentee will have to state and if necessary prove that the foreseeability requirement has been met. If the patentee fails to do so, the claim must be rejected.

So far the situation is, to us, clear. But what about the effective measures requirement? In order for his claims to be granted, does the patentee have to state and, if necessary, prove that the generic has *not* taken all the reasonably required effective measures? Or is it the generic who has to state, and if necessary prove, that they *have* taken all the reasonably required effective measures? The question here is whether the taking of effective measures should be regarded as a pure defence against the infringement, or as a liberating defence

[24] See Dijkman in his noot on the verdict in the BIE page 249.

[25] In the case that the generic claims a declaration that his product does not infringe, the situation is different.

against it. Is it (in the words of Verkade[26]) a "no, because defence" or a "yes, but defence"? If it is a "no, because defence", or a pure defence against the infringement, then it must be assumed that for the infringement it is not sufficient that the foreseeability requirement has been met. The patentee will also have to state and prove that the generic has *not* met the effective measures requirement. If we assume a liberating defence ("yes, but defence"), then it must be assumed that for infringement it is in principle sufficient for the patentee to state and prove that the foreseeability requirement has been met. The generic can then escape infringement (liberate themselves from it), by stating and proving that they have taken all reasonably required measures to prevent their compound from being delivered for the patented indication. The difference between a pure defence and a liberating defence is notoriously difficult in practice[27].
In MSD/Teva, the Supreme Court does not explicitly say anything about the burden of proof[28]. We tend to assume that relying on the effective measures requirement must be regarded as a liberating defence. We again cite the relevant part of consideration 3.4.4:

This is why it has to be assumed that a producer or seller only directly infringes a patent with Swiss-type claims when they foresee or should foresee that the generic product that they produce or offer will consciously be used for the treatment which the second medical indication patent concerns. For this it is required that the person skilled in the art based on the SmPC and/or the package insert, or through any other circumstances, will conclude that the product is (also) used or suitable for said treatment. The producer or seller will then have to take all reasonably required effective measures to prevent that his product will be distributed for the patented second medical indication. The mere presence – as in the current case – of a carve-out in the sMPC and package insert of the generic medicament is in general not sufficient to exclude the presence of direct infringement (HR 14 April 2017, ECLI:NL:HR:2017:692, NJ 2017/296, rov. 3.5.2). [emphasis added]

In our opinion, the Supreme Court indicates that a patent is infringed when the foreseeability requirement has been met ("only directly infringes"). They then seem to put the ball in the court of the generic, who has to take all of the reasonably required effective measures. This indicates, from our point of view, that the Supreme Court believes that the generic is responsible for proving that they took said measures. Therewith, this concerns a liberating defence. This is also logical since the generic knows what measures they took. It seems doubtful that the Supreme Court would dump this negative proof (being that the generic did *not* take all effective measures) on the patentee. We find further support for our point of view in the Sun/Novartis verdict of the Supreme Court[29]. In this case, Sun had put forward motivational complaints about the verdict of the Court of Appeal that Sun had failed to take effective measures to prevent that their generic medicament was issued through the health insurance company VGZ for an indication which was patented by Novartis. Sun complained, amongst other things, about the fact that the Court of Appeal had not made it clear which measures it was talking about. The Supreme Court rejected these complaints and considered the following (in English translation):

The judge is allowed to indicate measure that a party such as Sun in a case like this had to take, on the contrary, it rests on the party themselves to show what they have done to prevent infringement(...) [emphasiss added].

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[26] Conclusion Advocate Gernal Verkade at HR 15 December 2006, ECLI:NL:PHR:2006:AZ1083, NJ 2007, 203 (*NNEK/Van Mourik*).
[27] See for instance Th. Roëll, "Bewijslast voor beginners", Advocatenblad 2008, 498 – 503.
[28] The parties' debate might possible not directly have given opportunities for that.
[29] HR 14 April 2017, ECLI:NL:HR:2017:692.

This also indicates, in our opinion, that relying on the effective measures requirement has to be regarded as a liberating defence.

Should relying on the effective measures requirement be seen as a pure defence against infringement, then we believe that there is at least a certain provision of information duty (that is to say: a more stringent duty to state) of the generic to the patentee. To be able to judge if the measures that have been taken by the generic are all that can be reasonably required of them, and whether they are effective, the patentee obviously has to know which measures the generic has taken. The generic will have to inform the patentee of this.

The question remains whether all has been said on this matter. In this regard it helps to look at two different situations. In the first situation the generic medicament is basically issued on a large scale for the patented indication. The generic however shows that they have literally taken every imaginable measure to prevent this. We believe that following MSD/Teva that the generic goes free: no infringement. But, what about the opposite situation? The generic has taken no measures whatsoever, except a carve-out. Does this automatically mean that they are infringing or does the patentee still have to prove that the medicament is issued for the patented indication? Now, the patentee will always have to prove that the foreseeability requirement has been met, but what is foreseeable hasn't necessarily happened in practice. In MSD/Teva the Supreme Court does not require that the patentee proves that the medicament has actually been issued for the patented indication, so in a literal sense of the verdict the patentee does not have to prove this. This manner of reading the verdict in our eyes goes too far. We believe that in principle it can be desired of the patentee that they prove that the medication is (also) issued for the patented indication. Otherwise, he could get an injunction for an infringement which in practice has not occurred. In our eyes, this is different from the situation in which a patentee is trying to get an injunction to prevent the generic from introducing their medicament on the market. We will discuss this further under the heading "moment of assessment".

Advance notice to the patentee?

Does the generic have to inform the patentee of which measures they aim to take? Or is it sufficient to state that they have taken said measures and to state that the sales numbers of the patentee will show that said measures are effective? The Supreme Court is silent on this. We believe that in principle the generic has to inform the patentee in a timely manner of the measures they are going to take, or have taken, to prevent that their medicament is issued for the patented indication. In our opinion, this is a logical consequence of our conclusion that relying on the effective measures requirement is a liberating defence. Should it come to a proceedings, then the generic will have to state, and if necessary prove, that they have taken all measures that could reasonably be required of them. The patentee evidently has an interest to know what said measures are. That way, they can determine whether they believe that the generic has (possibly: for now) met the effective measures requirement. This way, a potentially unnecessary proceedings can be prevented. In case the generic refuses to inform the patentee in advance of the measures they have taken, this should in our opinion have consequence on the costs of the proceedings. We will discuss this further when we discuss the "moment of assessment". We regard informing the patentee of the measures taken as a measure itself that the generic could take to prevent infringement. We will discuss this further in paragraph 5.

Moment of assessment

The question of whether the effective measures requirement has been met could depend on the moment at which it is assessed. In this assessment it is relevant whether the medicament is already being offered and is procurable or not. Following jurisprudence, a patentee will only have sufficient (urgent) interest in proceedings against a generic product if the generic has committed an infringing act (or there is a concrete threat of impending infringement). As a general rule the admission of the

product in the Dutch medicament's pricelist ("G-standard") is the trigger for the patentee to start summary proceedings to prevent the generic medicament from actually entering the market[30]. The problem with this is that it cannot be properly assessed at that moment whether the measures that have been taken by the generic to prevent their medicament form being issued for the patented indication, are effective and whether they are all the measures that can be reasonably required of them. After all, the medicament is not being sold yet at that point in time. In such a case, the judge will have to estimate whether the effective measure requirement is expected to be met. This requires that during the summary proceedings the generic provides complete insight into the measures that they have taken. In our opinion, it wouldn't be right if the generic could get away by simply stating that they have taken sufficient effective measures and that this will become clear once the medicament enters the market, without indicating what said measures are. Furthermore, we are of the opinion that a generic that does not tell the patentee in a timely manner before the summary proceedings what measures they plan to take, they should carry the costs of the proceedings, even when the judge decides that the measures as such are effective (and consequently rejects the infringement claim). In such a case the proceedings could have been prevented if the generic had informed the patentee in advance. Informing the patentee in a timely manner is a simple measure that can be reasonably required of the generic. This allows the patentee to assess whether the measures, in their eyes, are sufficient. This also prevents that the patentee, due to a lack of transparency of the generic, starts summary proceedings to find out while the proceedings are pending that the measures were actually effective enough (and wouldn't have started the proceedings should they have known this in advance).

It is also possible that the judge has to assess the effective measures requirement when the product is already on the market. In that case, the judge, in our opinion, will have to assess in light of all circumstances whether the requirement has been met. We believe it should under certain circumstances be possible for both parties to ask the judge for a reassessment. An example. The patentee of a new-use patent starts summary proceedings against a generic immediately after publication of the G-standard. The preliminary relief judge rejects the claim because he judges that the measures that the generic is aiming to take will be sufficiently effective for now. Next, the medication enters the market and it turns out this judgement is incorrect. In our view, the patentee should be free in that case to address the preliminary relief judge in summary proceedings again to once again claim an injunction. Another possibility seems to be that the generic that wants to "play it safe" will initially take all different kinds of measures and later on comes to the conclusion that they could still fulfil the effective measures requirement with less measures. In these kinds of cases a reassessment should also be possible.

Type of patent

Finally, the question remains whether in the assessment of infringement on a new-use patent it is of relevance what type of patent it concerns (classic second medical indication, dosage regime, etcetera). The Supreme Court has given a clear judgement where it concerns the scope of protection. According to the Supreme court, in consideration 3.5, the type of patent is not relevant in this assessment. This is clear. Possibly, the type of patent could play a role in the question of what measures a generic can reasonably be expected to take, and whether such measures are effective. The question of which measures are effective, in our opinion depends on the specific circumstances of the case. The type of patent could potentially be relevant for that. With that, we have arrived at our discussion of the possible measure to take.

[30] According to the Dutch preliminary relief judges it is to the advantage of the patentee when they start summary proceedings when the generic product is not actually on the market yet. In that case, the patentee has a great interest in maintaining the status qua. See for instance Preliminary relief judge The Hague 1 March 2017, ECLI:NL:RBDHA:2017:1907 (*Eli Lilly/Sandoz*).

5. EFFECTIVE MEASURES

The verdicts of the Supreme Court in MSD/Teva and Sun/Novartis provide some support to determine when a generic has taken all reasonably required effective measures to prevent that their medicament will be issued for the patented new use. A handful of foreign decisions on this subject provide insight in the measure that a generic could take. We discern two questions: (i) which effective measures does a generic have at their disposal; and (ii) when has a generic taken all reasonably required measures in the Netherlands.

What effective measures does a generic have at their disposal?

In Dutch and foreign jurisprudence different measures are often mentioned that could be taken by a generic to prevent infringing on a new-use patent. Besides the ribavirin case (MSD/Teva) and the zoledronate case (Sun/Novartis), this also plays an important role in the pregabalin case (Lyrica®)[31].

Carve-out (skinny labelling)

Even though the use of a carve-out is in principle not enough to rule out (direct) infringement, the reverse is almost certain. Without a carve-out of the patented indication it appears that an effective infringement-defence is night impossible, so that simply said there is (at least) direct infringement of the new-use patent,

Writing the granting authorities

In the pregabalin case generics wrote the authorities that are responsible for granting market authorisations (in the Netherlands the College ter Beoordeling van Geneesmiddelen, "CBG") to request that they make known that the generic medication may only be prescribed for the non-patented indication. In Italy this has led to the AIFA (Italian equivalent of CBG) communicating through their website that the generic medicament will not be reimbursed in the event that it is prescribed for the patented indication. The granting authorities in Spain have similarly informed doctors and pharmacists. How this is being enforced by the authorities however is unclear. We are not aware of such announcements in the Netherlands and the chances that the CBG will make such announcements in the Netherlands seem slim to us.

Tenders with health insurance companies

In Sun/Novartis the participation of the generic (Sun) in a tender was the basis on which the proceedings rested. In this tender there was no differentiation between patented and free uses of the product. The Court of Appeal clearly states that the sole fact that the tender does not take (new-use) patents into account does not mean the generic goes free, since given the circumstances it should have been clear that the generic product would also be used for the patented use. On the contrary, according to consideration 4.34 it *was possible for Sun to do take all possible actions to prevent that the generic product would be issued for the treatment of osteoporosis, which would infringe on the patent of Novartis.*

In practice this means that one cannot simply hide behind the conditions of a tender if in the given circumstances it would be clear that the generic product could also be used in the patented use. The Court of Appeal also remarks in consideration 4.36 that the inability to participate in tenders is a circumstance that has to be taken up with the party that has written the tender (and is not a permit to infringe on patent rights).

The Oberlandesgericht Düsseldorf on 1 December 2015 has thus judged in a case between a health cost insurance company Kaufmännische Krankenkasse – KKH and Pfizer Pharma GmbH (also in a case about pregabalin Lyrica®)[32]. Here, the health cost insurance company was instructed to stop a pending tender procedure and to re-establish it in such a way that a distinction is made between free indications and patented indications. Further clarification

[31] See the verdict of the UKSC mentioned in the introduction. This case is still pending in several European jurisdictions including Germany and France.

[32] Oberlandesgericht Düsseldorf, decision of 1 December 2015 (ECLI:DE:OLGD:2015:1201.VII.VERG20.15.00).

of how the tender did have to be established follows from a second decision of the same Oberlandsgericht Düssledorf[33] about the same tender. From that it is clear that tender may not be designed in such a way that the patentee is excluded and that the health insurance company has to inform doctors about the necessity to prescribe the patented medicament for the patented indication.

We are not aware of jurisprudence in a comparable case in the Netherlands besides the mentioned Sun/Novartis case. We think it likely that the Dutch judge would see the "separation" of a tender procedure into patented and free uses of a medicament as a (possibly) effective measure in the sense of the MSD/Teva verdict.

Informing customers

A measure that the generic could take (and in our opinion in practice: should take) to prevent that their product is issued for the patented new indication, is informing customers. The generic has to provide information about the fact that (a) certain indication(s) is/are patented by a third party, and that this means that the product of the generic may not be issued for these indications.

From the considerations of the Court of Appeal in Novartis/Sun it follows that there are several requirements for this measure. In consideration 4.35 the Court of Appeal provides a few practical remarks on a letter that Sun sent to the wholesalers and hospital pharmacies. From those remarks we conclude that there are at least the following requirements:

- The letter has to make it explicitly clear that the issuing of the product for the patented treatment infringes on the new-use patent; and
- The letter has to be unambiguous and not suggest that this announcement does not have any practical meaning or does not require any measures (in this case ambiguity was caused by the opening sentence of the letter: "*This announcement only concerns a formality*")

Then the question is, who should such a letter be directed to. Is informing the direct customers (usually wholesalers and/or hospital pharmacies) enough, or is there a further duty of the generic to also address the parties further down the distribution chain? In our eyes, informing the wholesalers and/or hospital pharmacies should in most cases suffice. After all, in general the whole chain is supplied with the (generic) medicaments through these two channels. It is then up to the wholesalers to inform their clients about the (not) allowed uses of the medicament. Should the wholesaler not do so, or insufficiently do so, the patentee can notify the generic that the wholesaler is not informing clients and they can require the wholesaler to do so. Should the wholesaler still refuse to inform their clients, then the generic, where reasonably possibly, will have to address the matter themselves. In our opinion, it is preferred that the wholesaler has to inform clients themselves. The wholesaler is after all most aware of who he issues the medicament to and it seems desirable to us that it is prevented that pharmacies and doctors are flooded with letters from all sides. This does mean that both the patentee and the generic have to be able to force the wholesaler into action.

Applying information to the package

A measure that we have not come across in the jurisprudence, but that seems relatively simple for medicaments that are issued directly to patients via regular pharmacies, is the addition of a text on the packaging of the generic medication that it cannot be used for the patented indication. Consequently, it will still be clear that medicaments that end up in (regular) pharmacies without going through wholesalers are not to be used for the patented indication. Through this explicit warning regular pharmacies and patients (of whom it should be expected they know for which indication the medicament will be used) will be reluctant to still use the generic medicament for a patented indication.

[33] Oberlandesgericht Düsseldorf, decision of 11 May 2016 (ECLI:DE:OLGD:2016:0511.VII.VERG2.16.00).

Informing the patentee

In jurisprudence it has been assumed that a generic does not have a general duty to inform the patentee in advance about the launch of a generic product. This could cause some issues when it concerns a new-use patent, where the generic can only escape infringement when they meet the effective measures requirement. Here above, we argued that this means that the generic has to inform the patentee what measures they have taken. We are also of the opinion that it is logical based on MSD/Teva that the generic *does* have to inform the patentee of a new-use patent in advance about the launch of a generic product. In any case the informing should be weighed in the question of whether the generic has met the effective measures requirement. Informing in advance is after all also a reasonable (and even a very simple) measure to take. In our opinion you could even go a step further and say that one may expect that the patentee and generic will first try to reach an agreement about the way and content of the communication to the "market" and other measures to take. The interests of the (sincere) generic and the (sincere) patentee seem to run parallel after all.

The sincere patentee would mostly be interested in maintaining the profits of his patented indication, while the since generic should be focusing mostly on the free indication while wanting to prevent infringement on the patented part. An uncooperative patentee could be punished in the market, should a good mutual communication be lacking, by losing profits on the patented indication. On the other hand, an uncooperative generic would run a great risk of infringing on a patented indication. The attitude of both parties in the establishment of a message to the market and further measures could play a role in the answering of the question of whether a generic has met the effective measures requirement.

Market share after launch of the generic product and monitoring

Besides taking the measures before and during the launch of the generic product, is also seems important to monitor after the launch whether the generic product is not issued for the patented indication. In other words: were the taken measures effective? This means that generics have to keep a close eye on whether their market shares match the market share of the free indication(s). This will not always be simple and there could be competition law aspects that play a role. However, we believe that the generic does have an obligation to make an effort in this matter. The generic has to monitor whether this medicament is not still issued for the patented indication. The generic will have to respond to signals from the patentee in this regard. Should it be concluded that the generic product is not just incidentally issued for the patented indication (a.k.a the actual market share does not match the expected market share), then the generic in principle has to take action and take new measures, like informing wholesalers and pharmacies. The importance of such a measure is confirmed in for instance the decision of 13 October 2016 of the French preliminary relief judge in the Lyrica® case[34].

Other measures

It is very possible that due to the specific circumstances of the case the generic (also) can (and has to) take other measures to meet the effective measures requirement. For instance, the generic of an "expensive medicament", for which a so-called *add on* applies, could ask for an "add-on code" for only the non-patented indication[35]. What other measures apply (because they can reasonably be required of the generic and are effective) will depend on a multitude of factors, such as, the nature of the product, the manner of distribution, the method of administration, where administration occurs, the way in which the product is reimbursed, and so on.

[34] Tribunal De Grande Instance De Paris, 15/58725; decision of 13 October 2015.

[35] Shortly (although not entirely correctly) said, and add-on concerns a decision of the Dutch Healthcare Authority that a so-called expensive medication can be reimbursed.

When has a generic taken all reasonably required measures?

If a generic wants to rely on the effective measures requirement in the Netherlands, then they can choose from a large selection of measures. A few of these measures are, in our opinion, always necessary, while others strongly depend on the circumstances of the case. For instance, the SmPC of the generic medicament will definitely need to contain a carve-out. Besides that, the generic will, in our eyes, always have to abstain from participating in a tender without conditions from a health insurance company.

Writing to wholesalers and (hospital) pharmacies seems to be an effective measure. To which parties this correspondence has to be directed will depend on the type of medication. For an anti-cancer medication that is used only in a few specialised centres, it would be rather pointless to write to all the pharmacies in the Netherlands. For a medication that concerns the treatment of hay fever, it would be a completely different matter. In any case a generic should at least inform the patentee. A serious attempt of the generic to coordinate with the patentee in writing such a message and determining the further measures to take, should reinforce the generic's position.

Finally, we believe that continuing to monitor the (generic's) market share is of great importance. If it exceeds the share of the free indication, or if the generic finds out through different means that their product is not just incidentally prescribed for the patented indication, then the taken measures are obviously not effective (anymore) and thus the generic will have to take action. The generic should be required to take action as long as there are still measures that could reasonably be required to be taken.

6. CONCLUSION

The Supreme Court has given two criteria for the assessment of direct infringement, namely:

a) The foreseeability requirement: has the generic foreseen or should they have foreseen that the generic medicament will consciously be used for the patented treatment?

b) The effective measures requirement: has the generic taken all reasonably required effective measures to prevent that their generic medicament is issued for the patented indication?

In our eyes, the first criterion is easily met in practice. Exactly where the line is drawn for the second criterion is not yet clear: guiding jurisprudence after MSD/Teva is (still) missing. The measures mentioned her above give a generic a selection of more or less effective measures that they can take to ensure that their medicament is not issued for the patented indication. A completely foolproof system is however not provided through this. After all, the possibility remains that even without the generic's knowledge and outside their control, the generic medicaments are being issued for the patented indication. Due to the expected significant price difference between the generic medicament and the patented medicament, there will naturally be parties in the market that can profit from a "wrong" issuing of the medicament. A potential danger is that generics will decide to disregard a relatively small market like the Netherlands. Due to the ambiguities around the "effective" measures to take, the risk of infringement might be too big. This is an undesirable situation.

An important aspect of the problem we are describing is made up of the fact that the pharmacist (and the rest of the chain) does not know for what indication the doctor has prescribed the medication. We believe that a relatively small change in the current way of prescribing a medication could solve this problem for the most part.

Nowadays, prescriptions are not done using prescription notes anymore. General practitioners and hospital doctors currently use patient-information systems (such as a gp-information system) in which the data of the patients are registered, the doctor writes his reports, declarations are sent out, prescription are sent out and directly transmitted to the pharmacy. In a relatively simple way, we could upload into this system which indications a medication has been approved for (that is to say the indications from the SmPC). The doctor can then select the indication for which the prescription is issued and share this with the concerned pharmacy.

By providing a direct connection between the indication and the medicament, the pharmacy can easily determine whether a specific patient may be issued a generic medicament or whether they have to be issued the patented medicament. Should a pharmacy not follow this, then they are infringing. This requires health insurance companies to respect patent rights, and that they will back this system and support pharmacies that issue medications according to the system. Interestingly enough, this act of the doctor is already required for some medications (for the safety of the patient). The functionality is thus already present in these patient-information systems. It is also interesting to mention that Denmark already uses the system in such a way. But we are not there yet. Until then, generics and patentees in the Netherlands will have to make do with the mentioned (effective) measures.

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