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BIOSIMILARS AND BELGIAN PATENT DISPUTES (AS) IN SUMMARY PROCEEDINGS: "TO JUDGE, ONE MUST UNDERSTAND"*.

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OVERVIEW

Over the next decade, the basic patents of a large number of reference biologicals in Europe will expire at a increasing rate. Market analysts predict that a growing number of biosimilar medicines ("biosimilars") will be introduced commercially onto the European market, including Belgium. Or rather that is what the producers of biosimilars will attempt to do. However, it is likely that, the right holders to the reference pharmaceuticals will make every effort to prevent these biosimilars from entering the market, or at least remove them as soon as possible from it. The longer they can prevent increasing competition and retain their monopoly on these drugs, the longer they can charge higher prices, retain market share and ensure a return on investment. In Belgium, these right holders have countless resources at their disposal to achieve their goal, of which the best-known are probably counterfeit seizures and patent-based summary proceedings. Experience with the launch of generic pharmaceuticals in Belgium indeed shows that, as soon as one holds a European patent, most magistrates ruling (as in) summary proceedings presume that the invoked rights are *prima facie* valid. In these cases there is usually little room for discussion about the *prima facie* infringement, and the interests are (as far as this even happens) generally weighed in favor of the existing patent holder. The implications of this case law for the generic pharmaceutical companies, the users of the pharmaceuticals, and Belgian social security are enormous and a source of aggravation, especially when Belgium is the only country in the European Union where the generic drug in question is kept off the market.

As we will see in this overview, if this majority opinion within the Belgian courts is not reviewed, at least for biosimilars, then this issue will grow out of control. The expenses involved in the development and approval of biosimilars are easily ten, twenty and, according to some sources, sometimes more than fifty times higher than those for a generic pharmaceutical drug. These expenses clearly need to be recouped as soon as possible. Months, and sometimes even years of being kept off the market by a preliminary measure pending a decision on the merits can (sometimes literally) be a huge "mortgage" for the developers of biosimilars. It must also be taken into account that the sales price of a reference biological can amount to twenty to one hundred times that of a classical pharmaceutical drug. Reimbursable biological pharmaceuticals will thus exponentially increase the pressure on social security. So the Belgian state and tax payers would benefit from the price of these biologicals falling sooner rather than later as a consequence of biosimilar competition (figures based on H. GABROWSKI a.o. "The Market for Follow on Biologics: How Will it Evolve?", Health Affairs, vol. 25 (5), Sept/Oct 2006 and J. WINDISCH, "The Science in Biosimilars", Emergence of Biosimilar Medicines (symposium d.d. 22 November 2012, Belgian Federal Parliament).

At a political level, there is awareness that the path for biosimilar medicines has to become and remain paved (cf. speech of the European Commissioner Dalli, 18th EGA Annual Conference, 15th of June 2012), even if in Belgium it is a long and winding one (Senate 2012-2013, Written Question no. 5-7940 d.d. 23 January 2013). It is of crucial importance that, in time, these political efforts on a European and national level are not undone by biosimilars being treated in the same way as generic pharmaceuticals by the majority of the Belgian magistrates ruling on (as in) summary proceedings. This article seeks to outline what biosimilars are and how they differ from generic pharmaceuticals on one hand, and on the other, that the *prima facie* analyses can no longer occur as is the questionable case in most generic pharmaceuticals related patent litigation.

WHAT ARE BIOSIMILARS?

Biosimilars relate to biological pharmaceuticals ("biopharmaceuticals" or "biologicals") as a classic 'small molecule' chemical pharmaceutical relates to generic pharmaceuticals. For a good understanding of biosimilars, it is thus important to first describe what is understood by biologicals. A biological is a pharmaceutical in which the active component is a biological substance, meaning that the active component is produced by, or derived from, a living organism. It concerns a

very fast growing class of pharmaceuticals with which very serious and often even life threatening illnesses (cancer, diabetes, arthritis, etc.) can be treated with growing success.

Biosimilars are biological pharmaceuticals that are developed to be similar and even equivalent to existing biological pharmaceuticals (the 'reference pharmaceutical'). They are meant to treat illness in the same way as biologicals. In Europe it is (legally speaking) more correct to refer to these pharmaceuticals as "similar biological medicinal products" (cf. art. 10, fourth paragraph Directive 2001/83/EC of 6 November 2001 on the Community code relating to medicinal products for human use *Pb.L.* 28 November 2001, vol. 311, 67). In the United States they are rather referred to as "*follow-on-biologics*", while in Canada the term "*subsequent entry biologics*" is used. The World Health Organization refers to "*similar biotherapeutic products*". Many other terms are used too such as : biogenerics and biocomparables, for example.

BIOSIMILARS ARE NOT GENERIC PHARMACEUTICALS

In this article we use the term "biosimilars" and suggest that the term "biogenerics" is best avoided. Even though there are different terms for "biosimilars", most authors agree that there is a fundamental difference between biosimilars and generic pharmaceuticals (K. DE SMET, "Introduction to biosimilar medicines…", *De opkomst van biosimilaire geneesmiddelen, Symposium Belgisch Federaal Parlement*, 22 November 2012, 3; J. FREILICH, "Patent infringement in the context of follow-on biologics", *16 Stan. Tech. L. Rev.* 9, 2012, 20; X. "Barriers and opportunities for the uptake of biosimilar medicines in Belgium", *KCE Report* 199, 21). The applicable regulations require that generic pharmaceuticals contain the identical active ingredient as the reference pharmaceutical. Since the active ingredient of biosimilars and biologicals has its origin in living organisms, these ingredients are, because of their complexity (at least for what concerns the current state of the art), by definition not identical. This is because the active ingredient of biosimilars exists out of relatively large peptides or proteins with a complex 3D-structure and not out of one sole molecular entity, as is the case with conventional 'small molecule' pharmaceuticals (H. SCHELLEKENS, "Biosimilar therapeutics – what do we need to consider?", *NDT Plus* 2009, 2, suppl 1, i27-i36). In addition, these pharmaceuticals are usually produced in genetically modified cell lines that (because of, for example, post-translation modifications) impose their own variability in the development process. This heterogeneity applies when different 'batches' of the same biological are compared among themselves as well as when the biological and biosimilar are compared (D. CROMMELIN e.a., "Pharmaceutical evaluation of biosimilars: important differences from generic low-molecular-weight pharmaceuticals", *The European Journal of Hospital Pharmacy Science* 2005, volume 11, nr. 1, 11-17). It is not impossible that, because of for example, small differences in the production process (different pH, temperature, etc.), products are created that are not fully identical to those produced earlier with the exact same production process. The classic argument that generic pharmaceuticals are, by definition, infringing because they are necessarily identical to the reference pharmaceutical can therefore not be upheld for biosimilars. Even more than what should be the case with generic pharmaceuticals, the Belgian magistrates deciding (as in) summary proceedings must therefore leave room for an actual, be it *prima facie*, (non-)infringement debate.

There are even more differences between generic pharmaceuticals and biosimilars that are useful for understanding why existing case law cannot be applied blindly. The size ratio of a classic small molecule pharmaceutical compared to a biological pharmaceutical for instance, correlates to that of a grown man compared to six Eifel Towers that are stacked on top of one another (J. MACDONALD, "Introduction to biosimilars; From R&D to Product Registration", *Symposium Belgisch Federaal Parlement,* 22 November 2012, 4). The structure of a biological pharmaceutical is not only more complex, but also much weaker than that of a classic small molecule pharmaceutical, which makes it much more sensitive to external factors such as temperature. Furthermore the production processes for biological pharmaceuticals are much more complex and expensive than those for classic small molecule pharmaceuticals and they do not, as mentioned, deliver uniform but rather equivalent products. To guarantee the quality of biosimilars, they are subject to very stringent norms that must be respected before they are allowed to be commercialized. In essence these norms state that the biosimilar

must comply with the same quality guarantees as imposed on the biological that is the reference pharmaceutical (ex. clinical tests) and it must be demonstrated that the differences in the biosimilar are not of substantial importance for its quality, safety or efficacy. Besides these preclinical and clinical tests to illustrate the safety and efficacy of biosimilars for commercialization, the manufacturers of biosimilars also have to draft a comprehensive pharmacovigilance plan, related to the monitoring of possible side effects, even if they obtained the necessary marketing authorizations (F. LOCATELLI and S. ROGER, "Comparative testing and pharmacovigilance of biosimilars", *NDT* 2006, 21, suppl 5, v13-16). In classic pharmaceutical patent litigation, the patent holders often claim that weighing the interests of the parties is unnecessary or that their interest by definition outweigh those of the generic industry. A reason that is often invoked thereto is that the damage to the generic pharmaceutical companies is only in the form of slower or decreased sales and that this can, if necessary, be rectified through damages in the proceedings on the merits. Even though that is incorrect, it is clear already that for biosimilars, the damage discussion is much more complex, since the diverse investments that are required to commercialize a biosimilar are much more extensive and expensive than those for a generic pharmaceutical.

OBSERVATIONS ON PREVAILING CASE LAW

Prevailing case law concerning the treatment (as) in summary proceedings of generic pharmaceuticals cannot be realistically applied in full to biosimilars because of the fundamental differences between both types of pharmaceuticals. In this chapter it will be illustrated that, regardless of this difference, this case law is, at best, flawed.

When a manufacturer of a biological reference pharmaceutical wants to successfully enforce his rights on the Belgian part of a European patent in summary proceedings or through a counterfeit seizure, then essentially the same legal requirements should be fulfilled (disregarding the urgency requirement in preliminary injunction proceedings): (1) he should demonstrate that he can assert a *prima facie* valid patent; (2) that there is effectively a *prima facie* infringement of this title and; (3) that, after weighing all the interests concerned, the scales should tip in favor of the patent holder. It is therefore obvious from the start that it is insufficient to simply argue that one possesses an in Belgium correctly registered European patent.

A EUROPEAN PATENT IS NOT NECESSARILY *PRIMA FACIE* VALID

Applying a presumption of *prima facie* validity of a European patent in (as in) summary proceedings, is definitely no bad thing. These types of proceedings do not allow extensive examination of the invoked patent title. Such an examination would slow proceedings down too much. What is often forgotten though, is that the presumption of *prima facie* validity is a refutable presumption. In other words, when the party targeted by the patent holder has serious arguments to doubt the validity of the invoked right, then one can no longer grant preliminary injunctions by only referring to the fact that the patent holder has a European patent at its disposal. In that event, one should indeed establish exactly why the presumption remains in place, notwithstanding the arguments involved.

The foregoing may not be interpreted as if preliminary injunctions concerning patents are always exclusively justified by stating that the invoked European patent is presumed to be *prima facie* valid. Certain magistrates do concretely address the objections raised by the targeted party in their disposition (a good example of this can be found in Court of Commerce (Pres. (Sum. Proc.)) Antwerp 16 November 2010, *IRDI* 2010, issue nr. 4, 483). Too often though they limit themselves to giving standard reasons that do not always take reality into account. Below, a few recurring justifications are summed up and discussed as to why they are insufficient in many cases, especially when the dispute relates to biosimilars.

"The examinations by the EPO offer *prima facie* a sufficient quality guarantee"

It is regularly argued that European patents are only delivered after a thorough examination by experts and it can therefore be expected that the granting procedure at the EPO offers sufficient guarantees concerning the *prima facie*

validity (see Brussels 26 October 2010, *IRDI* 2011, 47-55, para. 21; Antwerp 25 April 2007, *IRDI* 2007, 248). Blindly applying this reasoning in all proceedings does not take account of reality. First of all, because the examiners of the EPO may certainly be very qualified professionals technically, but this does not guarantee that they are experts in every field. This cannot be expected of them. They must, even in their field of specialization, decide over inventions in so many sub domains, that they are forced to be good technical generalists, but not specialists. What may look like an invention to a generalist examiner of the EPO with a biotechnical background, can be entirely obvious to a professional in a pharmaceutical niche. Further it should not be overlooked that the EPO is an administrative institution which is under external pressure to (i) finish patent application procedures in the shortest possible time, which does not always allow a thorough investigation, and to (ii) grant a large amount of patents. It must also not be forgotten that the investigators can only base their verdict on information which is found in databases or which is given by the applicant itself (*infra*). They subsequently do not always know what is really actually known.

It is therefore hardly surprising that European patents are regularly granted incorrectly. The sector inquiry about the European pharmaceutical industry by the European Commission confirms that the majority of the European pharmaceutical patents are revoked in opposition procedures before the EPO. It also becomes apparent from the inquiry that in many cases the scope of protection is limited. In addition, it seems that after national invalidity proceedings, more than half of such patents are declared void. In other words, only 22% of these patents seem to be effectively valid, which puts the presumption of *prima facie* validity that is solely based on investigation by the EPO under serious pressure.

In certain cases this pressure is increased still further. There are known cases in which the examiners of the EPO had no knowledge of certain elements of the state of the art, on the basis of which the patent they had granted was subsequently declared void in non-Belgian proceedings. In certain cases it even concerned state of the art that originated from the patent applicant itself, who kept the latter secret from the examiners of the EPO. In such cases one can no longer hide behind the presumption of *prima facie* validity and the patent holder must quickly and convincingly demonstrate that, notwithstanding this state of the art that was kept hidden, his patent is indeed still *prima facie* valid (*contra*: Pres of the Court of Commerce of Brussels (*MSD vs Sandoz*; RK 00119/2010), 19 October 2010, *not published*; Court of Commerce of Brussels (*Sandoz vs MSD*; AR A/10/6898), 21 February 2012, *not published*. On the grounds of a study of MSD (that the examiner of the EOB did not know of) the Court of Commerce of Brussels revoked the preliminary injunctions that had been obtained in summary proceedings a year and a half earlier by MSD on the basis of its European patent. Whereas the judge in summary proceedings did not even answer the arguments that Sandoz put forward, the judge in the proceedings on the merits concluded that the study belonged to the state of the art, rendering the concerned patent obvious). At that point, the patent holder should obviously not develop a comprehensive validity argument. This would not only imply that there are no convincing, concise counterarguments, but it would also go beyond the scope of (as in) summary proceedings.

"That there is still opposition before the EPO is irrelevant"

In certain cases the *prima facie* (non-)validity of European patents has to be decided by Belgian judges even though the patent holder is still fully involved in opposition proceedings before the EPO. It even occurs often that the Opposition Division reverses the findings of the examiner and revokes the patent or limits it considerably. In Belgian patent-related (as in) summary proceedings, the revocation of a patent during the opposition proceedings seldom has any influence on the presumption of *prima facie* validity. As a result of the ruling of the Belgian Supreme Court (Cour de Cassation / Hof van Cassatie) of 5 January , 2012 (*IRDI* 2012, vol. 3, 262) judges feel more confident than ever in their belief that a patent holder can continue relying on the *prima facie* validity up until the moment where the patent is definitively revoked (Brussels 25 March 2013 (AR 2012/KR/127, *Bayer vs Sandoz*) with reference to Brussels 26 October 2010, *RABG* 2011, 31). According to this case law, the Belgian Supreme Court ruled that the decision of the Opposition Division, which went to appeal before the Technical Boards of Appeal, had no legal consequences for the apparent rights of the patent holder,

and this as long as no ruling on the merits of the case had been handed down. This interpretation of the ruling is, first of all, wrong: the Belgian Supreme Court ruled that the decision of the Opposition Division, which was appealed, does not necessarily have legal consequences for the rights of the patent holder. It is thus still up to the judge who rules on the merits of the case to verify case by case, *prima facie*, how likely it is that a decision of the Opposition Division will be upheld in appeal (see also V. CASSIERS, note under Cass. 5 January 2012, *Ing. Cons.* 2012, 213). It is important that the judge keeps in mind that the presumption of *prima facie* validity of European patents is based on the quality of the examination of the state of the art by the examiner of the EPO. If the Opposition Division decides that this very same patent must be revoked, then the EPO decides in essence that its examiner should not have granted the patent. Frequently this same examiner is part of the panel of the Opposition Division that revokes the patent (art. 19 EPC). In these cases it is the examiner himself who admits that the patent should never have been granted. Even if an appeal against this verdict before the Technical Board of Appeal has a suspensive effect, the verdict of the Opposition Division cannot simply (i.e. without giving specific reasons) be ignored by the Belgian judge ruling (as in) summary proceedings (especially considering the broad degree of discretion the judge in (as in) summary proceedings enjoys). He must, certainly in the context of weighing of interests (*infra*), take it into account, even if the appeal before the Technical Board of Appeal has suspensive effect. This is even more so when on the grounds of article 15 (1) of the Rules of Procedure of the Technical Boards of Appeal in the invitations for the hearing, there are already indications that the claimed *prima facie* valid patent will be limited or revoked. The presumption will receive a final blow when the Technical Boards of Appeal revokes the patent or limits it substantially, even if the patent holder can still appeal to the Enlarged Boards of Appeal at that moment.

"Only the Belgian part of the patent is up for discussion. Foreign case law is irrelevant"

In pharmaceutical patent disputes, Belgium typically is one of the markets where proceedings are only initiated once similar cases have been argued (and often ruled upon) abroad, (for example in the United Kingdom, Germany, etc). Regularly there are therefore already judgments of foreign (and often specialist) judges available, who in a well-argued manner rule on the (non-)validity of inventions that were patented. Just as frequently these foreign rulings are ignored in Belgian proceedings. It is then argued that in cases ruled upon in other countries there was no ruling on the Belgian part of the European patent and that it is this Belgian part of which the *prima facie* validity needs to be debated. This argument is frequently combined with the argument that Belgian judges are not bound by foreign judgments and/or that an analysis of this foreign case law exceeds the limits of a *prima facie* ruling (Antwerp 1 February 2013 (2012/AR/486, *Roquette t Syral*) *not published*).

This opinion should not be accepted. It undermines all efforts of leading patent judges to strive for consistency across Europe and for more uniform European patent-related case law (see for ex. High Court of Justice (Patents Court), London 27 November 2012 (HC12E02962 and HC12A03340, *Actavis – Medis v. Eli Lilly*), nr. 100; Court of Appeal of England & Wales 15 October 2010 ([2010] EWCA Civ 1110, *Grimme v. Scott*), nr. 80 and R. EBBINK, "Beschermingsomvang in Nederland anno 12 – Hoge Raad 25 May 2012 (AGA/Occlutech)", *IE-Forum.nl*, nr. 11514, 1). This 'island'-mentality is even more regrettable in light of (albeit, or better: moreover) English case law which states very clearly that important foreign rulings should, in principle, be followed. In addition, the opinion threatens the credibility of the way Belgian patent disputes are handled in summary proceedings. When a patent relating to the same invention as the one which must be *prima facie* evaluated in Belgium, is deemed void in (almost) all the countries in which proceedings took place, the Belgian courts cannot simply ignore this by stating that they are not bound by these judgments. It is correct to say that they are free to decide the case, but then it must be made clear in the ruling why they disagree with all of these decisions. Simply stating that this would exceed the scope of the *prima facie* discussion will not do. Essentially, if a majority of foreign judgments decide and explain why a patent is void on the basis of uniform European patent law, which must also be applied by Belgian judges, the presumption of *prima facie* validity of a centrally granted European patent title expires. It will then be up to the patent holder to convince the Belgian judge, with clear arguments that require no extensive

analysis, that all these foreign judges were wrong. This is also the opinion of the foreign case law to which was referred to earlier. According to this case law, even one important foreign ruling is enough to bind other judges, unless it is proven that the first judge made a mistake in the evaluation of the invoked patent and/or the infringement thereof (cf. Court of Appeal of England & Wales 15 October 2010 ([2010] EWCA Civ 1110, *Grimme v. Scott*), nr. 80).

Finally it must be emphasized that a holder of a biological patent cannot escape this burden of proof by referring to the fact that there is an appeal against (a) negative foreign judgment(s) (*contra*: Antwerp 1 February 2013 (2012/AR/486, *Roquette t Syral*, *not published*). They will still have to clearly prove why this/these judgment(s) is/are wrong and why it/they will be overruled in appeal. The often referenced and discussed Belgian Supreme Court judgment of 5 January, 2012 offers no solace on the matter, since the Belgian Supreme Court only ruled on the procedural rules of the EPO (suspensive effect of an appeal against a decision of the Opposition Division) and not on the (foreign) civil procedural rules.

Conclusion in regard to *prima facie* validity

Clearly, it is not appropriate to consider that the Belgian part of a European patent, despite the fact that it is seriously disputed, is *prima facie* valid and justifies granting provisional measures for the protection of this patent, as long as it was not declared void by a decision that is no longer open to appeal. The *prima facie* validity of the Belgian part of European patents is, and remains, a refutable presumption. Such refutation will occur if it is proven that one or especially several of the following elements are in place:

- to a skilled person it is obvious that the examiner of the EPO made a scientific mistake;
- the examiner did not examine certain elements of the state of the art when studying the patent application that led to the patent in question;
- the Opposition Division revoked or substantially limited the patent (if the examiner who initially granted the patent is part of the panel of the Opposition Division, this argument should be deemed more important);
- the Technical Boards of Appeal revoked or substantially limited the patent;
- in another jurisdiction, the counterpart of the Belgian part of the patent has been declared void on the basis of the EPC and the motivation seems *prima facie* not to contain any mistakes.

If it appears that the patent holder cannot prove concisely with clear and convincing arguments that what happened does not adversely affect the presumption of *prima facie* validity, then the (as in) summary proceedings judge must grant the alleged infringer the benefit of doubt.

A BIOSIMILAR IS NOT NECESSARILY *PRIMA FACIE* INFRINGING

"In summary proceedings there is no room for discussion concerning infringement"

Bearing in mind the high development costs of biosimilars as outlined earlier, manufacturers will always want to execute a thorough risk analysis before launching a biosimilar on the Belgian market. This risk analysis will probably even be performed before the actual development of the biosimilar begins. It should appear from this analysis that the biosimilar can be launched in a sufficient number of markets without risk, so that the enormous investment in the development of the biosimilar is guaranteed and can start generating a return as soon as possible. Such risk analysis for the Belgian market is only possible when Belgian courts develop a uniform and consequent case law, so biosimilar manufacturers can adapt their market behavior to it. This is particularly the case for summary proceedings. These hold the risk that the access to the Belgian market is closed in the extreme short term and for many years to come (i.e. as long the proceeding on the merits (at least in first instance) are ongoing). If this predictability is seen to be impossible or if it seems that there is no

room for a real debate about the infringement, as is now often the case in summary proceedings for generic pharmaceuticals, then the risk exists that various biosimilars will not be developed, or at least not be made available in Belgium. Since making biosimilars unavailable can have a considerable impact on (the cost of) public health, judges (in summary proceedings) should not deal with the infringement debate in a frivolous manner (Antwerp 13 July 2011, *IRDI* 2011, 329).

"The pharmaceutical in question is by definition infringing"

In the (*prima facie*) infringement debate, the following rule of thumb with respect to the burden of proof relating to a claimed patent infringement should be remembered: the burden of proof lies completely with the patent holder (M. BUYDENS, *Droit des brevets d'invention,* n° 390). In classical infringement (as in) summary proceedings concerning generic pharmaceuticals, this burden of proof is very light, since the patent holder can invoke the legal requirement that generic pharmaceuticals contain the identical active ingredient as the reference pharmaceutical (cf. definition of "generic pharmaceutical" in art. 10, B of Regulation 726/2004). For biosimilars it is, at this point not technically possible to guarantee that they are completely identical to their biological counterpart. It is even impossible to guarantee this for different batches of the same biological pharmaceutical, produced by the same manufacturer. The biological complexity of these pharmaceuticals indeed makes it impossible for biosimilars to be regarded as copies. The issue of proving *prima facie* infringement however also pops up elsewhere. Because of their complexity, the production process of a biosimilar allows quite a bit of variation, without there being a different product than the reference biological pharmaceutical for what concerns the market authorization. Indeed, variations are possible on the level of pretransformation (e.g. different promoters), the transformation (e.g. changes in cell lines), the cell structure (e.g. different temperature), the purification (e.g. different purification method) and the formulation (e.g. different inactive ingredients such as buffers) (J. FREILICH, o.c., 28).

These characteristics of biosimilars imply that in essence there is no room left for a *prima facie* debate about a literal patent infringement, and that discussions about infringement by way of equivalent will gain substantial importance. This doctrine allows the patent holder to act against alleged counterfeit, in which not all characteristics of the patent are found identically, but in which these were replaced by obvious technically equivalent characteristics (F. GOTZEN and M.C. JANSSENS, *Wegwijs in het intellectueel eigendomsrecht*, Bruges, Vanden Broele, 2012, 267). To verify whether there is such a technical equivalent, Belgian courts usually apply (implicitly or not) the "function-way-result"-test. With this test it is verified whether the essential characteristic of the patent, which is not identifiable in identical manner in the alleged counterfeit, was replaced by a means that substantially fulfills the same function in substantially the same way and with substantially the same technical result (P. DE JONG, O. VRINS and C. RONSE, "Evoluties in het octrooirecht Overzicht van rechtspraak 2007-2010", *TBH* 2011, 419).

Having to (mandatorily) resort to the theory of equivalency has a few important consequences for the *prima facie* appreciation of the (non-)infringing character of the biosimilar:

- Because of arguing infringement by way of equivalent, the patent holder himself admits that he cannot demonstrate literal patent infringement. The patent holder must invoke the theory of infringement by way of equivalent to be able to accuse the manufacturer and/or distributor of the biosimilar of patent infringement. If there is no literal infringement, it can hardly be said that the (literal) infringement is *prima facie* clear. On the contrary, *prima facie* it seems that the accused process/product does not fall under the claims of the patent in question.
- However, there is an additional (and more important) consequence. Verifying whether there was an infringement by way of equivalent demands "a very thorough technical and legal investigation concerning the existence of an infringement [that goes] outside the scope of a summary proceedings" (Brussels 3 November 2008, IRDI 2009, 351, nr. 54). In order to verify whether there is an infringement by way of equivalent, one needs to define the essential

characteristics of the patent on the basis of the descriptions and drawings. This evidently requires a thorough study and interpretation of the concerned patent (including the state of the art at the moment of the patent application). Only in the second phase, when all the technical characteristics have been identified, can the doctrine of equivalence be applied (B. VANDERMEULEN and R. PEETERS, "De equivalentieleer in de Belgische octrooirechtspraak", IRDI 2003, 133). As confirmed by the afore-mentioned judgment of the Court of Appeal of Brussels, it goes without saying that this two-steps analysis cannot happen *prima facie* in the context of summary proceedings. This is even more the case when this analysis takes place in a technically complex domain such as biological pharmaceuticals. One cannot expect in summary proceedings that, before ruling, the judge will extensively study what the state of the art was, how the claimed invention differs from the state of the art, how the claimed infringing product, let alone the claimed infringing process differs from the claimed invention and subsequently if these differences would effectively be deemed negligible by a skilled person. If the patent holder does not have sufficient unelaborated arguments to immediately convince the preliminary injunction judge of the infringement on his patent, then "there is insufficient appearance of rights to justify the requested measures." (Brussels 3 November 2008, IRDI 2009, 351). In the drospirenone judgments of 25 March, 2013 the Court of Appeal of Brussels deviated from its nevertheless clear point of view from 2008 concerning the *prima facie* review of infringements by way of equivalent (Brussels (Bayer vs Sandoz AR 2012/KR/127) and Brussels (Bayer vs Effik Benelux, AR 2012/KR/132, IRDI 2013/3, 32. Although the claimed infringers in these proceedings explicitly referred to the Court's judgment of 2008, the Court of Appeal of Brussels did not give any reason why in the drospirenone cases there was room to apply the doctrine of equivalence in summary proceedings. Because of a lack of clear reasons this matter still remains undecided.

Conclusion in relation to the *prima facie* infringement

On the basis of the above, many manufacturers and distributors of biosimilars should see (as in) summary proceedings decided in their favor. This would be an acceptable outcome in most cases. Bearing in mind the particularly complex character of the infringement question in biosimilar related summary proceedings, it is most unlikely that the judge will rule with complete and accurate knowledge of all the elements of the case and it is therefore perhaps better that he does not rule on the matter. The judges in question could, for example, decide that a correct analysis and an answer of the infringement question goes beyond the scope of summary proceedings. In my opinion the judge ruling (as) in summary proceedings can only conclude that there is infringement when there have been (multiple) decisions from leading patent jurisdictions abroad that already established the infringement (preferably on the merits). In that account it is in the interests of unambiguous European patent case law, that uniformity on a European-wide level is reached as far as possible (*supra*).

THE INTERESTS AT RISK DESERVE A CORRECT INTEREST CONSIDERATION

In view of the interests at stake, the conclusions pertaining to the *prima facie* validity and infringement are not surprising. When a judge in summary proceedings effectively takes into account all the interests at stake, then the patent holder will seldom be able to assert more than a pure financial interest. If in the future, be it after a debate on the merits of the case, it appears that this interest was indeed violated, then a full indemnisation is almost always possible through damages. This cannot be said when the interest of the manufacturer and/or of the distributor of the biosimilar was violated, let alone when it is established that the general interest suffered from the unjustly granted preliminary prohibitory injunctions.

The judge in summary proceedings must indeed also safeguard public interest. It that respect the expense of biological pharmaceuticals should be recalled. The reimbursement of a biological pharmaceutical will increase the pressure on social security at an unprecedented rate. The general interest, more specifically that of the Belgian State, the tax payers and the patients in question, can only benefit from biosimilar competition pushing the cost of biological reference

pharmaceuticals downwards. Hence, political efforts are being made nationally, as well as at European level, to clear the path for biosimilars. These efforts should not be derailed by placing preliminary injunction obstacles in the way. This is particularly so now that the patent holder generally should not fear a claim for damages by the concerned stakeholders when in the proceedings on the merits the patent holder is found to be wrong. This debate is very complex and is, because of the high expenses and especially because of the small amount of damages awarded, often not pursued. Therefore it is up to the judge to protect the public interest in this context.

In addition, there are also the interests of the manufacturers of the biosimilars to take into account. A significant difference with manufacturers of generics, is that manufacturers of biosimilars normally only produce a few and frequently only one product. Before they can produce and market a biosimilar, these companies have to invest considerable sums in research and development, as well as in meeting the regulatory requirements and other associated costs. This by itself already entails a significant commercial risk. However when it appears that a return on the investment involved is unlikely within a reasonable timeframe, for example because of a preliminary prohibitory injunction, then these companies not only stand to incur considerable losses, but their continued existence is also endangered. If during the proceedings on the merits, it appears that the patent holder was unjustly awarded a preliminary prohibitory injunction, the (curator of the) biosimilar manufacturer is faced with an impossible situation. The damage suffered by a possible bankruptcy of a biosimilar manufacturer is almost incalculable. Even if the manufacturer of the biosimilar in question survives the impact of the preliminary injunction, the judge on the merits of the case will be confronted with an impossible debate about the suffered damage, taking into account the endless amount of hypotheses and variables which must be considered (loss of reputation, slower growth in market share, loss of potential sales, missed potential to reinvest profits etc.). It is extremely difficult to quantify the extent of the damages, both existing and the future potential damages, all of which weigh heavily in the context of interest consideration (D. LINDEMANS, *Kort geding*, Kluwer, Antwerpen, 1985, 85). As previously mentioned, these elements gain even more importance when it appears that the Opposition Division of the EPO or foreign judges revoke the patent, render it void or limit it considerably.

Opposite the general interest and that of the biosimilar manufacturers and/or distributors is the interest of the patent holder. In disputes on generic pharmaceuticals, it is nearly always argued that the patented invention must be protected because of the extensive investment incurred during the research and development phase. The idea is that the patent holder is, in principle, entitled to obtain the best economic return from the investment by means that would include the temporary exclusion of competition. This argument is of less significance in disputes concerning biosimilars. As outlined earlier, there are investments linked with the development of biosimilars that are on a similar scale as for the patent holder in question. On this level interests are balanced. In addition, the patent holder has usually had the opportunity to make a return on his investment. Producers of biosimilars will not be inclined to make their products commercially available before the basic patent(s) of the reference biological pharmaceutical has/have expired. During this period, the patent holder thus enjoys a monopoly. Additionally the manufacturer of a biosimilar will not be able to acquire a marketing authorization before the exclusivity period ("date exclusivity period") has expired (art. 10 Directive 2001/83/EC). Essentially, this means that the biological reference pharmaceutical has to be authorized to enter the market for at least ten years before another company can offer the biosimilar on the market (X, *o.c.*, 27). During this period, the patent holder can harvest the fruits of his patent monopoly. If this monopoly comes to an end because of the rejection of a preliminary prohibitory injunction in summary proceedings, and the patent holder is forced to lower his prices and also loses market share, then the caused damage (especially compared to the damage of the manufacturer of biosimilars) is easier to define. Indeed, every sold infringing biosimilar remains easily traceable (for a similar reasoning for generic pharmaceuticals: Brussel 15 June 2004, *IRDI* 2005, vol. 1, 67).

Finally, it must be pointed out that the rule of proportionality is often overlooked in (as in) summary proceedings case law. This rule states that the more extensive the (as in) summary proceedings claimed measures are, the more clearly the rights of the parties need to be vested (S. BEERNAERT, "Algemene principes van het civiele kort geding", *RW* 2001-02,

1348-1349). A counterfeit seizure and particularly a preliminary injunction can generate the following consequences: access to confidential information by a direct competitor, *de facto* product recall, and inaccessibility of the market during the long duration of the proceedings on the merits, among others. If such measures are claimed by the patent holder, the judge of the summary proceedings will have to analyze the invoked patent and the claimed infringement *prima facie* but critically and (s)he will also have to clearly mention the grounds for her/his decision. This is even more the case when the patent holder requests such measures merely on the basis of a *prima facie* infringement by way of equivalent (as far as the (as in) summary proceedings judge will consider himself having jurisdiction for this matter).

CONCLUSION

Globally, courts that have jurisdiction over patent disputes are facing enormous challenges in relation to biosimilars. This is particularly true for the Belgian magistrates competent for patent based summary proceedings and counterfeit seizures, primarily because it is up to them to create a clear and unambiguous case law for biosimilars in Belgium. This implies that they have to take Belgian case law and that of foreign judges in comparable cases into consideration, as well as take into account what foreign judges may have already ruled on the patent in dispute, and the claimed infringement. Only in this way can a qualitative European patent case law be developed and can biological reference pharmaceutical patent holders, as well as biosimilar manufacturers/distributors, bring their market behavior in line with case law. Patent holders can already take certain precedents into account during the drafting of their patent (application)s. The manufacturers/distributors of biosimilars can do the same when developing their launch strategy and even during the decision-making process in which it is decided whether or not to invest in the development of a certain biosimilar. The fact that the biosimilars are a scientifically-technically complex subject matter and that the legal questions that they raise are not always easy to answer, should not be a reason for Belgian magistrates to simply copy the case law concerning generic pharmaceuticals. Indeed, as outlined above, besides the fundamental differences between the two types of pharmaceuticals, the economic and social interests at stake are too important for this.

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