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4b O 39/18

Pronounced on 1 October 2018

Beihof, Judicial Officer

as Registrar of the Court

Regional Court Düsseldorf

IN THE NAME OF THE PEOPLE

Judgement

In the preliminary injunction proceedings

Merck Sharp & Dohme Corp., represented by their CEO Kenneth Frazier, 126 East Lincoln Avenue, 07065 Rahway, N.J., US,

Injunction Plaintiff,

Attorneys of record: Law Firm Hogan Lovells International LLP, Kennedydamm 24, 40474 Düsseldorf,

v e r s u s

ratiopharm GmbH, represented by its managing directors Christoph Stoller, Andreas Burkhardt, Dr. Miran Denac, Graf-Arco-Str. 3, 89079 Ulm,

Injunction Defendant,

Attorneys of record: Law Firm Bird & Bird, Großer Grasbrook 9, 20457 Hamburg

Civil Division 4b of the Regional Court of Düsseldorf through the Presiding Regional Court Judge Dr Voß, Regional Court Judge Dr Thom, and Regional Court Judge Terlinden

has r u l e d as follows after the oral hearing held on 11 September 2018:

I.

That the preliminary injunction of the Regional Court of Düsseldorf of 16 May 2018 be revoked. The motion for injunctive relief is dismissed.

II.

The costs of the proceedings will be borne by Injunction Plaintiff.

III.

The judgement is preliminarily enforceable. Injunction Plaintiff may ward off execution by providing security in the amount of 110% of the amount to be executed, unless Injunction Defendant provides security in the amount of 110% of the respective amount to be executed prior to execution.

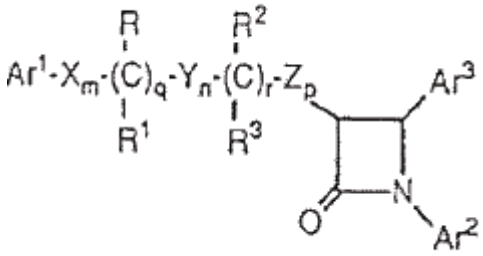
Facts of the case

Injunction Plaintiff is suing Injunction Defendant for an injunction due to alleged infringement of the supplementary protection certificate DE 12 2004 000 026.1 (hereinafter referred to as: Injunction Certificate II).

Injunction Plaintiff was the holder of the European Patent EP 0 720 599 B1 (hereinafter referred to as: "Basic Patent", cf. Exhibits HL 5, 5a), granted in English with effect for the Federal Republic of Germany, which was filed on 14 September 1994 while claiming a priority date of 21 September 1993. The granting of the Basic Patent was published on 19 May 1999. The Basic Patent expired on 14 September 2014. The Basic Patent concerns the hydroxy-substituted azetidinone compound ezetimibe, or pharmaceutically acceptable salts thereof, and the combination of ezetimibe with a cholesterol synthesis inhibitor.

Claims 1 and 8 of the Basic Patent read:

1. Compound represented by the formula



or a pharmaceutically acceptable salt thereof, wherein

Ar1 and Ar^2 are selected independently from the group consisting of aryl and R^4-substituted aryl,

Ar^3 is aryl or R^5-substituted aryl,

X, Y and *Z* are selected independently from the group consisting of $-CH_{2-}$, -CH(C_1-C_6 alkyl)- and -C(di(C_1-C_6) alkyl),

R and R^2 are selected independently from the group consisting of $-OR^6$, $O(CO)R^6$, $-O(CO)R^9$ and $-O(CO)NR^6R^7$,

R^1 and R^3 are selected independently from the group consisting of hydrogen, C_1 -C_6 alkyl and aryl

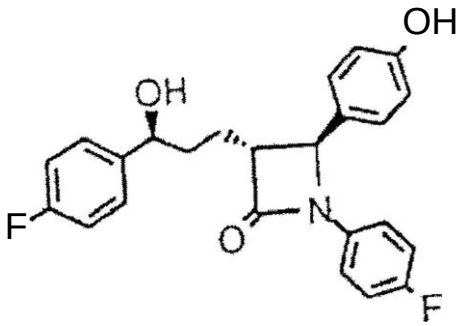
q is 0 or 1; r is 0 or 1; m, n and p are independently 0, 1, 2, 3 or 4; provided that at least one of q and r is 1, and the sum of m, n, p, q and r is 1, 2, 3, 4, 5 or 6; and provided that, when p is 0 and r is 1, the sum of *m,* q and n is 1, 2, 3, 4 or 5;

R^4 is 1-5 substituents independently selected from the group consisting of C_1-C_6 alkyl, $-OR^6$, $-O(CO)R^6$,$-O(CO)OR^9$,$-O(CH_2)_{1-5}-OR^6$, $O(CO)NR^6R^7$, $-NR^6R^7$ $-NR^6(CO)R^7$ $-NR^6(CO)OR^9$, $-NR^6(CO)NR^7R^8$ $NR^6SO_2R^9$ $-COOR^6$, $CONR^6R^7$, $-COR^6$, $SO_2NR^6R^7$, $S(O)_{0-2}R^9$, $O(CH_2)_{1-10}$, $-COOR^6$, $O(CH_2)_{1-10}CONR^6R^7$, $-(C_1$-C_6 alkylene)$COOR^6$, $-CH=CH-COOR^6$, -CF3, CN, NO_2 and halogen;

R^5 is 1-5 substituents independently selected from the group consisting of OR^6, -O(CR)R^6, $-O(CO)OR^9$, $-O(CH_2)_{1-5}OR^6$, $-O(CO)NR^6R^7$, $-NR^6R^7$, $-NR^6(CO)R^7$, $-NR^6(CO)OR^9$, $-NR^6(CO)NR^7R^8$, $-NR^6SO_2R^9$, $-COOR^6$, $-CONR^6R^7$, $-COR^6$, $-SO_2NR^6R^7$, $S(O)_{0-2}R^9$, $-O(CH_2)_{1-10}COOR^6$, $-O(CH_2)_{1-10}CONR^6R^7$, $-C_1C_6$ alkylene)$COOR^6$, and $CH=CH-COOR^6$,;
R^6, R^7 and R^8 are independently selected form the group consisting of hydrogen, C_1C_6alkyl, aryl and aryl-substituted C_1-C_6alkyl, and

R^9 is C_1-C_6 alkyl, aryl or aryl-substituted C1-C6 alkyl, wherein aryl is phenyl, naphthyl, idenyl, tetrahydronaphthyl or indanyl.

8. Compound in accordance with claim 1, represented by the formula



or a pharmaceutically acceptable salt thereof.

In Claims 9 to 16, the combination of a compound of hydroxy-substituted azetidinones such as ezetimibe is protected with a cholesterol biosynthesis inhibitor. Specific inhibitors are named in Claim 17.

Claim 9 reads:

> A pharmaceutical composition for the treatment or prevention of atherosclerosis, or for the reduction of plasma cholesterol levels, comprising an effective amount of a compound as claimed in any one of claims 1 to 8, alone or in combination with a cholesterol biosynthesis inhibitor, in a pharmaceutically acceptable carrier.

Claim 17 reads:

> A pharmaceutical composition of claim 16 wherein the cholesterol biosynthesis inhibitor is selected from the group consisting of lovastatin, pravastatin, fluvastatin, simvastatin, CI-981, DMP-565, L- 659,699, squalestatin 1 and NB- 598.

After a merger with the original holder Schering Corp, Injunction Plaintiff is the holder of the Injunction Certificate II (since 18 June 2013, in any case), granted for the Basic Patent with effect for Germany. The Injunction Certificate II protects the product "ezetimibe or pharmaceutically acceptable salt thereof in combination with Simvastatin". It was applied for on 22 June 2004 and granted on 4 April 2005.

The approvals of Injunction Plaintiff's drugs INEGY®, GOLTOR®, VYTORIN® and ZEKLEN®, which contain ezetimibe and simvastatin as their active ingredients, served as permits to bring those drugs onto the market on 2 April 2004.

The granting of Injunction Certificate II was published on 29 May 2005. Injunction Certificate II has been effective in the Federal Republic of Germany since 15 September 2014 and will presumably expire on 2 April 2019 (cf Exhibit HL 1). Multiple nullity actions against Injunction Certificate II are pending before the Federal Patent Court.

Moreover, Injunction Plaintiff's legal predecessor was the holder of the supplementary protection certificate DE 103 99 001.1 (not contested here) for the substance "ezetimibe or pharmaceutically acceptable salt thereof"

(hereinafter referred to as: "Certificate I"). Certificate I was also registered on the basis of the Basic Patent. It was the basis of the permit for placing the active ingredient ezetimibe (EZETROL®) on the market. Its term ended on 17 April 2018.

Injunction Defendant is one of the largest manufacturers of generic drugs on the German pharmaceutical market. Injunction Defendant has already received a drug approval for its preparation ezetimibe/simvastatin ratiopharm (hereinafter referred to as: "challenged embodiment"), which constitutes a generic version of the preparation INEGY®. The challenged embodiment exists in four compositions, with 10 mg of ezetimibe and 10, 20, 40 or 80 mg each of simvastatin (cf Exhibit HL 9).

Regarding Injunction Plaintiff's written request to stop selling the challenged embodiment before the term of protection for Injunction Certificate II (cf. Exhibit HL 12) expired, Injunction Defendant did not react accordingly (cf. Exhibit HL 13), but pointed out that it believed the Injunction Certificate II was null and void.

Injunction Plaintiff believes that the legal validity of the injunction certificate is qualified as sufficiently certain. In particular, the injunction certificate is not null and void, because all the conditions of Article 3 of Regulation (EC) no. 469/2009 (hereinafter referred to as: SPC Regulation) were met.

The product claimed in the injunction certificate, the combination of ezetimibe and simvastatin as well as both single ingredients, are named in the claims of the Basic Patent (Art. 3 a) SPC Regulation). The combination of ezetimibe and simvastatin is an independent product for which no SPC has been granted (Art. 3 c) SPC Regulation): Before the priority date, the combination of statins (such as simvastatin) with other cholesterol reducing ingredients, such as the hydroxy-substituted azetidinones (such as ezetimibe), which have not been researched further to date, was not typical, due to the side effects which arose.

On 27 April 2018, Injunction Plaintiff learned from the journal "Deutsche Apotheker Zeitung" [German Pharmaceutical Newspaper] that the challenged embodiment in the version from 26 April 2018 was advertised as available "immediately". That party

then immediately filed the motion for injunctive relief.

At Injunction Plaintiff's request, the chamber granted a preliminary injunction with a resolution on 16 May 2018, which prohibited Injunction Defendant from offering drugs containing ezetimibe or pharmaceutically acceptable salts thereof in combination with simvastatin, especially the preparation ezetimibe/simvastatin ratiopharm, in the Federal Republic of Germany, bringing those drugs onto the market, using them, or introducing them or possessing them for the purposes mentioned. The preliminary injunction was delivered to Injunction Defendant's attorneys of record on 25 May 2018. With a pleading dated 2 July 2018, Injunction Defendant objected to the preliminary injunction.

Injunction Plaintiff requests that

> the preliminary injunction of the Regional Court of Düsseldorf of 16 May 2018 be upheld.

Injunction Defendant moves that

> Injunction Plaintiff's request dated 14 May 2018 to issue a preliminary injunction be rejected and the preliminary injunction dated 16 May 2018 (File No. 4b O 37/18) be revoked.

Injunction Defendant believes that the Injunction Certificate II will not prove to be legally valid.

For an SPC to be granted for a combination of ingredients, that combination must be tied to an independent, central inventive step (core inventive advance) which goes beyond the normally protected mono-ingredient (Art. 3 c) SPC Regulation). Only such a product is entitled to compensation for the delay in commercial exploitation. To that end, the only thing that must be examined is whether the ingredient realises the Basic Patent's inventive concept. The invention's only subject matter lies in the

provision of ezetimibe. Certificate I was already granted for that purpose. The combination of ezetimibe and simvastatin is not an additional independent subject matter of the invention of the basic patent. At no place in the Basic Patent are there any tests or experimental evidence of the effectiveness of such a combination. Apart from that, a trend for doctors to combine simvastatin with other ingredients existed before the priority date. Furthermore, it was already generally known that simvastatin inhibits the body's own cholesterol synthesis by inhibiting HMG-CoA-reductase and hence has a mode of action complementary to that of azetidinone derivatives (such as ezetimibe).

In addition, combining ezetimibe and simvastatin does not give rise to an additive effect.

Within the context of Art. 3a SPV-VO, it also depends on the two ingredients of the product reflecting the inventive core of the Basic Patent.

Moreover, the earlier, first approval for the drug EZETROL® from 2002 expressly included the combination of ezetimibe and simvastatin, so that the condition of Art. 3d SPC Regulation is no longer met.

And Injunction Plaintiff has lost the overwhelming number of parallel procedures abroad in Europe.

The exceptional circumstances required to grant the injunction would not be constituted. In particular, calculating any damage compensation claim of Injunction Plaintiff would not bring about great difficulties, since the revenues with drugs can be accessed in publicly accessible databases, and the damage incurred by Injunction Defendant would be significant and irreparable.

Ultimately, there is no urgency. Injunction Plaintiff must have known before 11 April 2018 that the challenged embodiment was listed in the Lauer-Taxe pharmaceutical database. This is revealed by an email of the IFA GmbH dated 11 April 2018. Injunction Plaintiff should have already taken action at this time.

To that extent, Injunction Defendant disputes for lack of actual knowledge that Injunction Plaintiff first learned on 11 May 2018 that the challenged embodiment was listed in the Lauer-Taxe pharmaceutical database.

As regards the further details of the matter and status of the dispute, reference is made to the pleadings exchanged between the Parties, along with the documents submitted for the record and the protocol of the oral hearing of 11 September 2018.

Grounds for the decision

Following the admissible objection, the issued preliminary injunction must be dismissed.

During the further course of the proceedings, Injunction Plaintiff has failed to make any grounds for the injunction credible, Sections 935, 940 ZPO in conjunction with Sec. 139 para. 1 of the Patent Act (PatG) in conjunction with Art. 64 EPC in conjunction with Art. 5 SPC Regulation. It is true that Plaintiff has an injunction claim to a cease-and-desist action regarding the infringement of the Injunction Certificate II (under I). However, the Chamber believes that the injunction certificate will not prove to be legally valid, so there is no reason for the injunction (under II.). Therefore, we can find no overriding interest of Plaintiff in maintaining the injunction (under III.).

I.

Plaintiff has an injunction claim to a cease-and-desist action regarding the infringement of the Injunction Certificate II, Section 139 para. 1 PatG in conjunction with Art. 64 EPC in

1.

The Basic Patent underlying Injunction Certificate II concerns an invention relating to pharmaceutically active substances that belong to the group of azetidinones, as well as the combination of a hydroxy-substituted azetidinone and a cholesterol biosynthesis inhibitor, to treat and prevent atherosclerosis. The azetidinones of the invention are hypocholesteremic agents, i.e. cholesterol-reducing agents (cf. Exhibit HL 5a, para. [0001]; hypercholesterolaemia leads to atherosclerotic coronary artery disease. Atherosclerosis is the main reason for illnesses of the

coronary artery system and the most frequent cause of death in the Western world (cf. Exhibit HL 5a, paragraph [0002]). Therefore, the goal of the research is to prevent the formation of cholesteryl esters—the main way in which cholesterol accumulates in arterial walls—and reduce serum cholesterol (cf. Exhibit HL5a, paragraph [0003]). The human organ which is mainly responsible for balancing and regulating the cholesterol level is the liver. Among other things, it is responsible for building up (biosynthesis) and breaking down (catabolism) the cholesterol-containing lipoproteins in plasma. In the liver, lipoproteins of very low density are formed and eliminated. These are metabolised into low-density lipoproteins in the circulation system. The increase of low-density lipoproteins in plasma leads to increased atherosclerosis (Exhibit HL5a paragraph [0006]). If the intestinal absorption of cholesterol is reduced by a hypocholesteremic compound, less cholesterol will be added to the liver. This produces fewer lipoproteins of very low density, so, accordingly, fewer low-density lipoproteins can be formed through metabolism. At the same time, the unabated breakdown of low-density lipoproteins in the liver (catabolism) causes the plasma's cholesterol level to sink (cf. Exhibit HL5a, paragraph [0007]). The Basic Patent protects new hypocholesteremic compounds known as "hydroxy-substituted azetidinone compounds", which inhibit the absorption of cholesterol through the intestines and significantly reduce the formation of hepatic cholesterol esters (cf. Exhibit HL 5a, paragraph [0009] ff.), especially the active ingredient ezetimibe. Moreover, the Basic Patent protects a combination of hypocholesteremic compounds (which inhibit the absorption of cholesterol through the intestines) and statins (which inhibit cholesterol biosynthesis) (cf. Exhibit HL 5a, paragraph [0027]).

Claim 1 of the Basic Patent comprises a group of substances which feature the characteristic 4-azetidinone ring. The general formula in claim 1 of the Basic Patent includes ezetimibe in general. Dependant claims 7 and 8 identify ezetimibe specifically. Ezetimibe is illustrated through the structural formula in claim 8 (see above). Furthermore, the Basic Patent claims the combination of a compound in accordance with claims 1 to 8—hydroxy-substituted azetidinones such as ezetimibe—with an inhibitor of cholesterol biosynthesis (statin), claims 9 and 12 to 18. Claim 17 addresses

a selected group of cholesterol biosynthesis inhibitors, including simvastatin.

Certificate I was granted for the product ezetimibe or pharmaceutically acceptable salts thereof. Injunction Certificate II, which is still in effect and forms the subject matter of this dispute, was granted for the product ezetimibe or pharmaceutically acceptable salts thereof in combination with simvastatin.

2.

It is undisputed that the challenged embodiment is a drug which combines the ingredients ezetimibe and simvastatin and is protected by the Injunction Certificate II. Therefore, the injunction certificate has been breached. Furthermore, the risk of repetition needed for the cease-and-desist claim also exists, since Injunction Defendant has already offered the challenged embodiment for the purposes of Sec. 9 PatG.

Moreover, Injunction Plaintiff has failed to make a reason for the injunction credible.

1.

The issuance of an injunction can only be considered if both the issue of a patent infringement and the validity of the protective right on which the injunction is based ultimately have to be answered in favour of Injunction Plaintiff so that an erroneous decision cannot seriously be expected that may have to be revised in subsequent main proceedings. Normally, this can only be expected if the injunction patent has already survived opposition or nullity proceedings in the first instance.

In order to make a protective right for which an injunction is sought suitable for preliminary injunction proceedings, a positive decision regarding legal validity made by the competent opposition or nullity courts having the relevant technical knowledge is generally required. However, such a decision can be dispensed with in special cases, according to local established case law (cf. to that end Higher Regional Court of Düsseldorf, GRUR-RS

2018, 1291 - Rasierklingeneinheit). A "special case" can be assumed, for example, if (considering the market situation or the imminent disadvantages arising from the breach of the protective right) extraordinary circumstances are constituted which make it unfeasible for Injunction Plaintiff, as an exception, to wait for the outcome of the pending opposition or nullity proceedings (Higher Regional Court of Düsseldorf I-2 U 17/17, judgement from 14.12.2017).

Such a circumstance is usually the case during infringement proceedings involving generic drug manufacturers (cf. Higher Regional Court of Düsseldorf, GRUR-RR 2013, 236 - Flurpirtin- Maleat). Therefore, the Higher Regional Court of Düsseldorf considers the damage caused by generic drug manufacturers if the patent is later upheld to be enormous and, due to the drop in prices, irreparable, whereas an unjustified injunction can result merely in an illegal prohibition of market entry, which can be fully compensated by damage compensation claims, whereby, aggravating the situation, the generic drug manufacturer has generally incurred no economic risks through its market presence, but was able to benefit from the clinical tests and market establishment of the plaintiff's preparation (cf. Higher Regional Court of Düsseldorf, BeckRS 2016, 06353). Therefore, a prohibitory order must be issued, even if no previous ruling has been made in opposition or nullity proceedings, if the infringement court (due to the estimation possible for that court in light of the technical materials concerned) is convinced, within the meaning of sufficient credibility, that the protective right upon which the injunction is based is legally valid, since the lack of patentability will not allow the object of the protective right's invention to be determined. To that end, from the viewpoint of the infringement court, either the better argument must speak for patentability, so that it can be affirmed, or the question of patentability must remain at least unclarified considering the distribution of the burden of proof in the legal validity proceedings, so that the infringement court, if it had to decide the matter instead of the Patent Office or Federal Patent Court, would have to affirm its legal validity (Higher Regional Court of Düsseldorf, BeckRS 2016, 06353).

These principles must also be transferred to the situation of an injunction certificate whose legal validity is contested, since its normal purpose is to extend the Basic Patent to compensate for the virtual reduction of the duration due to lengthy drug approval procedures, and to give the certificate holder the opportunity to

amortize its research investments (cf. recital (4) of the SPC Regulation). The risk distribution previously depicted applies to the situation of the injunction certificate similarly.

2.

Judging by these principles, the Chamber is convinced that the Injunction Certificate II will not prove to be sufficiently legally valid. The odds are that the Injunction Certificate II will be declared null and void, Art. 15 Abs. 1 a) SPC Regulation. Although the contested product ezetimibe in combination with simvastatin is protected by the Basic Patent (Art. 3 a SPC Regulation; see a), a certificate—Certificate I—has already been granted to that end. This means that the condition of Art. 3 c) SPC Regulation has not been met. The case law of the CJEU establishes the certificate-specific requirements of the invention's core as part of Art. 3 c) SPC Regulation. The combination ezetimibe/simvastatin does not constitute the invention's core under the Basic Patent (see b).

a)

The product "ezetimibe or pharmaceutically acceptable salts thereof in combination with simvastatin" is protected by the Basic Patent, which was in effect on the date on which the Injunction Certificate II was filed.

aa)

The contested combination of the ingredients ezetimibe and simvastatin constitutes a "combination of active ingredients" for the purposes of Art. 1 b) SPC Regulation. "Active ingredients" are substances intended to be used as medically effective components when drugs are manufactured, or to become medically effective components of those drugs when they are used during the drug manufacturing process (Sec. 4 para. 19 of the Medicinal Products Act). Both ezetimibe and simvastatin are used as active pharmaceutical ingredients in the preparation INEGY®. To this extent, the contested combination of active ingredients is a product for the purposes of Art. 1 b) SPC Regulation.

bb)

This product must be protected by a Basic Patent which was in effect when the injunction certificate was filed (Art. 3a SPC Regulation). This means that a Basic Patent is a patent that protects a product as such (Art. 1c)).

In recent years, the CJEU has been involved in various questions referred with interpreting the product protected by a Basic Patent as such. Among national states and the authorities and courts concerned there with the individual cases at hand, there is still disagreement regarding the understanding of the CJEU, which is evident not least from these proceedings.

Based on the current case law of the CJEU, the Chamber comes to the following understanding regarding Art. 3 a) SPC Regulation: a product for the purposes of Art. 3 a) SPC Regulation is protected by a Basic Patent as long as the patent claims necessarily and specifically relate to this product, even if it is not expressly mentioned in the claims. For the purposes of this provision, a product consisting of multiple active ingredients with a combined effect is protected by an effective Basic Patent if the claims of that Basic Patent necessarily and specifically relate to the combination of active ingredients of which the product consists, even if they are not expressly mentioned. So from the viewpoint of the person skilled in the art, and according to the prior art on the submission date or the priority date of the Basic Patent, the combination of active ingredients must necessarily be included in the invention protected by the patent in light of the patent's description and drawings, and each active ingredient must be specifically identifiable in light of all the information disclosed by the patent (cf. CJEU, judgment of 25 July 2018 - C-121/17, Teva/Gilead). The test of whether the combination is necessarily included in the invention protected by the patent is to be made in accordance with Art. 69 EPC and the written report about its interpretation (cf. CJEU, GRUR 2014, 163 - Eli Lilly/HGS). To this extent, the CJEU continues its case law in the case "Medeva", according to which the combination of active ingredients must be specified in the claims of the Basic Patent (cf. CJEU, GRUR 2012, 157 - Medeva). The Basic Patent and its claims must be interpreted, and it must be determined to what extent the combination of active ingredients is protected by the Basic Patent as a subject matter of the invention. In so doing, it is not ruled out that a Basic Patent might protect multiple, different products (cf. CJEU, GRUR 2014, 157 -

Actavis/Sanofi, marg. no. 29). The Chamber does not infer from the ruling Actavis/Sanofi (CJEU, GRUR 2014, 157 - Actavis/Sanofi) any superordinate examining step within the framework of Art. 3 a) SPC Regulation, according to which the combination must be examined for its core inventive advance (cf. Meier-Beck, GRUR 2018, 257; elsewhere BPatG, GRUR 2014, 1073 - Telmisartan). This is already spoken against by the fact that the inventive step affects patentability, which can be judged exclusively on the basis of national law or European contract law (cf. Schlussanträge Wathelet dated 25 April 2018, Legal Matter C- 121/17, Teva/Gilead).

In any case, as far as the requirements of Art. 3 a) SPC Regulation are concerned, the Chamber does not deviate from the opinion of the 4th Nullity Senate of the Federal Patent Court (cf. BPatG, resolution dated 28 August 2017, File No. 4 Ni 20/17, Exhibit HL 14). In another case concerning a combination of active ingredients, the Senate states that, in its opinion, the product or active ingredient or combination of active ingredients must recognisably form the subject matter of the invention, which must be determined through interpretation. To this end, in turn, the technical teachings specifically embodied in the claim are crucial, as the person skilled in the art would understand if observing without bias the patent specification while drawing on his pre-understanding and the overall disclosure (Exhibit HL 14, p. 18).

Regarding the prerequisite of Art. 3a SPC Regulation, the Senate distinguishes between two partial aspects which it considers decisive when determining whether a combination of active ingredients constitutes a product that is protected by an effective Basic Patent: first, the pharmaceutical conditions under which (a) a product can be specified by interpretation as a subject matter of the invention; and second, the patent-law criteria according to which (b) the active ingredient should be specified (cf. Exhibit HL 14, p. 22). The Senate understands among the necessary pharmaceutical prerequisites that if the active ingredient is only functionally outlined, it should be deemed protected by the Basic Patent only if the active ingredient objectively falls under the umbrella term, and it can be simultaneously ruled out that other active ingredients might also constitute the same type of representatives of the umbrella term although they do not share the specific pharmaceutical qualities of the active ingredient designated (cf. Exhibit HL 14, p. 24). As the specific medicinal effect of the designated active ingredient increases, the Senate believes that the opportunity wanes to consider that ingredient as sufficiently functionally outlined through a broad umbrella term. In a second step

it must be determined in accordance with common principles of interpretation whether the sufficiently specified active ingredient is to also be recognised as a protected subject matter of the invention. Whether the technical teachings make a statistic or dynamic statement must be examined (cf. Exhibit HL 14, p. 27). The latter is the case if the inventive content already lies in the generic teachings of the use of a certain group of active ingredients, whereby the Senate supports itself on the decision "Dipeptidyl-Peptidase-Inhibitoren" of the BGH (BGH, GRUR 2013, 1210).

In the case at hand, it must already be considered at this point that, unlike the case to be assessed by the 4th Nullity Senate, the active ingredient simvastatin can be understood not only as included in the umbrella term cholesterol biosynthesis inhibitor in claim 9, but, beyond that, is specifically named in claim 17.

dd)

The claims of the Basic Patent specifically refer to the combination of ezetimibe with simvastatin. The very wording of claim 9 explicitly involves a pharmaceutical composition consisting of ezetimibe (claim 8) in combination with a cholesterol biosynthesis inhibitor. The cholesterol synthesis inhibitor is further specified in claim 16 as an inhibitor selected from the group consisting inter alia of HMG-CoA-reductase inhibitors. Claim 17 further specifies the inhibitor as simvastatin, which is explicitly named from the group of HMG-CoA-reductase inhibitors along with nine other statins.

The person skilled in the art would infer from the general description (paragraph [0027], Exhibit HL 5a (= paragraph [0016], Exhibit HL 5)) that the invention also refers to a procedure to reduce the plasma's cholesterol level and a treatment procedure to prevent atherosclerosis. The procedure consists of administering a combination of a cholesterol absorption inhibitor in the form of a hydroxy-substituted azetidinone of Formula I and a cholesterol biosynthesis inhibitor to a mammal needing such treatment. The same paragraph re-emphasises the "combined use" of the cholesterol absorption inhibitor with a cholesterol biosynthesis inhibitor. In the following paragraph [0028] (= paragraph [0017]), the patent names another aspect of the invention: the pharmaceutical composition, comprising a quantity of a cholesterol absorption inhibitor in the

form of a hydroxy-substituted azetidinone of Formula I, a cholesterol biosynthesis inhibitor and a pharmaceutically acceptable carrier. This combination is already addressed in paragraph [0001] up to the pharmaceutical carrier. In paragraph [0049] (= paragraph [0028]), the person skilled in the art learns that one example of a HMG-CoA-reductase inhibitor is the active ingredient simvastatin, which is even preferred. In paragraph [0093] (= paragraph [0066]), the Basic Patent suggests a dosage for HMG-CoA-reductase inhibitors normally considered to be once or twice a day, 10 to around 40 mg per dose, which would equal a daily dose of 10 to 80 mg.

Thus, the Basic Patent addresses the specific combination of active ingredients both in the claims and in the description. From the prior art that the Basic Patent addresses in paragraph [0008], the person skilled in the art is aware that statins—such as HMG-CoA-reductase inhibitors—represent an effective way to reduce plasma cholesterol. To this extent, it is clear to the person skilled in the art according to his expert knowledge that using simvastatin as a statin competitively inhibits a liver enzyme (HMG-CoA-reductase) which is responsible for the speed of the cholesterol biosynthesis. The inhibition, by using high regulation and reduced breakdown of the LDL receptors in the liver, causes the LDL cholesterol to be removed from the circulatory system (cf. privately obtained expert opinion Assmann dated 24 August 2015, marg. no. 26, Exhibit HL 6a; privately obtained expert opinion Assmann dated 22 May 2018, marg. no. 26, Exhibit HL 18a). Due to his general expert knowledge, the person skilled in the art was also aware of the risk that monotherapy with statins entails: side effects such as liver damage and the destruction of muscle fibres (cf. privately obtained expert opinion Assmann dated 24 August 2015, marg. no. 30, Exhibit HL 6a; privately obtained expert opinion Assmann dated 22 May 2018, marg. no. 30, Exhibit HL 18a). He is also aware from the state of prior art that a reduction of intestinal cholesterol absorption will cause less cholesterol to be added to the liver (paragraph [0007], Exhibit HL 5a). Here, the active ingredient to be combined—the azetidinone ezetimibe (claim 8)—is used. Ezetimibe inhibits a special protein that settles mainly in the gastrointestinal tract, which leads to reduced intestinal intake of cholesterol (cf. privately obtained expert opinion Assmann dated 24 August 2015, marg. no. 35, Exhibit HL 6a). To this extent, the person skilled in the art will recognise that by combining the active ingredients ezetimibe and simvastatin, each will achieve an additive effect. Ezetimibe reduces the intake of LDL cholesterol in the gastrointestinal tract, and simvastatin is responsible for the increased breakdown of LDL cholesterol in the liver. The reduced amount which

is added to the liver and the accelerated breakdown in the liver strengthens the reduction of LDL cholesterol. Although this advantage is not explicitly named in the Basic Patent or experimentally proven, the person skilled in the art will recognise that the combination can strengthen reduction of LDL cholesterol.

Therefore, the contested combination constitutes a specific part of the technical teaching of the Basic Patent, and therefore a protected product in and of itself for the purposes of Art. 3 a) SPC Regulation. The Chamber does not currently expect the Federal Patent Court to reach another conclusion in its two-stage examination. If nothing else, because the objective medicinal requirements of a sufficient specification through the express mention of the active ingredient simvastatin have been fulfilled.

b)

However, the condition of Art. 3 c) SPC Regulation has not been met. Certificate I has already been granted for the contested combination of active ingredients ezetimibe and simvastatin, because ezetimibe represents the sole subject matter of the protected invention in a certificate-specific sense. The combination of the active ingredients ezetimibe and simvastatin does not constitute the core of the Basic Patent's technical teaching (see aa), which must be given a separate protection certificate (see bb). Neither does this assessment oppose the differentiated picture painted by the case law of the member states (see dd).

aa)

According to the purpose and rationale of the supplementary protection certificate, the regular term of the Basic Patent on which the granting of the certificate is based should be extended along with the certificate. With the supplementary protection certificate, only the de facto restoration of a sufficient period of effective protection of the Basic Patent is sought, in that, after the expiry of his patent, the holder is granted an additional period of exclusivity which is intended, at least in part, to compensate for the delay in the commercial exploitation of his invention that has occurred from the filing of the patent application until the granting of the first marketing authorisation for the European Union.

(cf. for the preceding Higher Regional Court of Düsseldorf, judgement of 6 August 2015, File No. I-2 U 21/15 with reference to CJEU, GRUR 2015, 658 - Actavis/Boehringer; GRUR 2015, 245 - Forsgren/Austrian Patent Office; GRUR 2014, 163 - Eli Lilly/Human Genome; GRUR 2014, 157 - Actavis/Sanofi). The duration of the approval procedure will be compensated, but not its expense.

The extension should be made only once, since a certificate may not have been granted for one and the same product (cf. Art. 3 c) SPC Regulation). So only one supplementary protection certificate should be granted per product, which is understood in a more narrow sense as an active ingredient (of combination of active ingredients) (cf. CJEU, GRUR Int. 2014, 149 - Georgetown University/Octrooicentrum Nederland). If the Basic Patent protects various products, more supplementary protection certificates may be granted for each of those various products, provided each of those products is protected "as such" by the Basic Patent for the purposes of Art. 3 a) SPC Regulation (CJEU, GRUR 2015, 658 - Actavis/Boehringer Ingelheim, marg. no. 33; GRUR 2014,157 - Actavis/Sanofi, marg. no. 29).

In its rulings Actavis/Sanofi (GRUR 2014, 157) and Actavis/Boehringer Ingelheim (GRUR 2015, 658), the CJEU independently defines what it means by protection "as such". Art. 3 c) SPC Regulation in circumstances in which a supplementary protection certificate was already granted for a new type of active substance based on the protective patent and an approval for the marketing of an individual formulation that contains it which made it possible for the patent holder to object to the utilization of this active substance, alone or in combination with other active substances, is to be interpreted in such a way that it is, according to this regulation, not permitted to grant the holder based on the same patent, but a later approval for the marketing of another pharmaceutical product which contains the named active substance together with another active substance which is as such not protected by the patent, a second supplementary protection certificate for this active substance combination (cf. CJEU, GRUR 2014, 157 - Actavis/Sanofi marg. no. 43). Within the framework of Art. 3 c) SPC Regulation, the CJEU also points out that the product (the active ingredient/the combination of active ingredients) "as such" constitutes the central advance of the invention covered by the Basic Patent. The product should be the core of the invention (CJEU, GRUR 2014, 157 - Actavis/Sanofi, marg. no. 30). The active ingredient must form the sole subject matter of the invention protected by the patent (CJEU, GRUR 2015, 658 - Actavis/Boeringer Ingelheim, marg. no. 38 et seq.). Even if the result of the interpretation of the Basic Patent is that it

protects the product (the active ingredient/the combination of active ingredients) in accordance with Art. 3 a) SPC Regulation, the product in accordance with Art. 3 c) SPC Regulation is entitled to a supplementary protection certificate only if it constitutes a core inventive advance on the priority date (cf. CJEU, GRUR 2014, 157 - Actavis/Sanofi).

To that end, the Chamber does not believe it is necessary for the active ingredient/the combination of active ingredients to be entitled to an independent inventive step in isolation, with the result that the inventive step would need to be reviewed as part of Art. 3 c) SPC Regulation. Such an understanding can be ruled out due to the same arguments that were cited in connection with Art. 3 a) SPC Regulation. The inventive step exists under the postulate of the respective national law of the member state, which is relieved of the decision-making competency of the CJEU. The Chamber therefore also avoids translating the expression "core inventive advance" with "central inventive step", since this comes all too close to equality with inventiveness. The term used by the CJEU must be seen in the context of the SPC Regulation. It must be comprehended autonomously, from a purely patent-law perspective. With this term, the CJEU takes account of the fact that the delay in commercial exploitation is to be compensated only for the part of the invention that makes up the core of the inventive step constituting the subject matter of the Basic Patent (CJEU, GRUR 2014, 157 - Actavis/Sanofi, marg. no. 41). In so doing, the CJEU accepts that the economic losses are only partially amortized, since the SPC Regulation does not aim to compensate for delays to their full extent or regarding all possible forms of exploitation of the inventions, such as in the form of various compositions with the same active ingredient (CJEU, GRUR 2014, 157 - Actavis/Sanofi, marg. no. 31,41).

A supplementary protection certificate must be due to a section of the Basic Patent that must also embody the actual technical achievement. This is a part of the invention formed by the core of the Basic Patent's technical teaching. If multiple active ingredients are combined, that very pharmaceutical composition must solve a specific problem during the healing, prevention or diagnosis of illnesses. The Basic Patent must address this problem, but at least the technical solution for the problem that constitutes an effect other than that associated with the single active ingredient, by the priority date.

Thus, the requirement of the invention's core constitutes a valuation under the law governing protection certificates (Meier-Beck, GRUR 2018, 657; similar to Brückner/v. Czettriz, supplementary protection certificates, 2nd ed. 2014, Art. 3 AM-VO marg. no. 456: a "valuable impediment [...] against misuse of the regulation"). It serves as corrective purpose, to avoid the risk of having to grant a number of supplementary protection certificates for ever new sections of the protected invention which, however, do not form the main component of the lengthy and costly research work.

A purely additive effect from two combined active ingredients, in which the combination of active ingredients achieves the same therapeutic effect as the separate administering of both active ingredients, doesn't satisfy the CJEU as the sole subject matter of the invention (cf. CJEU, GRUR 2014, 157 - Actavls/Sanofl). And the Federal Patent Court also seems to view a delineation between additive and synergistic effects as a useful distinction criterion, even if it doesn't focus on the core of the invention—unlike the Chamber as part of Art. 3 c) SPC- VO—but situates the aspects of invention quality in the interpretation of the Basic Patent in the context of Art. 3 a) SPC Regulation. For example, in the preliminary opinion dated 28 August 2017 (Exhibit HL 14, p. 21), the Federal Patent Court expressly leaves the question open of where exactly the delineation between patentable combinations of active ingredients and independent subject matters of inventions is to be found by way of interpretation, with the note that, in the case the court was reviewing, the straight active ingredients "even" generated a synergistic effect compared to the mono-ingredients.

Moreover, the Chamber feels that, besides the synergistic effect, other modes of action are conceivable for a combination of active ingredients which can form the core of the invention protected by the Basic Patent. A mode of action which helps reduce side effects and makes administration easier can absolutely constitute the core of the subject matter of the invention if it is different from the mode of action of the mono-ingredients. But for that to happen, the Basic Patent must contain reliable indications on the priority date that prove that the combination of active ingredients will achieve this form of effect. The Chamber believes it is insufficient, according to the stipulation from the CJEU presented above, if the effects do not arise until during the approval procedure. For the duration of the approval procedure is

not compensated by a supplementary protection certificate if certain effects are only discovered after the priority date through clinical studies and are not previously obvious to the person skilled in the art from the Basic Patent. For, from the viewpoint of the SPC Regulation, this is no longer a product that is protected "as such" (i.e., with these effects) by the Basic Patent. Ultimately, it is difficult for certain effects to constitute the sole subject matter of the invention of the Basic Patent, which the person skilled in the art would expect based on his general expertise because they occur periodically (for example, that a "fix dose" in a single table improves compliance with patients and to this extent makes dosing easier).

bb)

According to these principles, the combination of ezetimibe and simvastatin does not constitute a product as such which embodies the central advance protected by this Basic Patent. The invention's core is only to provide the new active ingredient ezetimibe. But Certificate I has already been granted for this product. To this extent, the prerequisite in accordance with Art. 3 c SPC Regulation for granting Injunction Certificate II has not been met.

(1)

The present case constitutes the arrangement already judged by the CJEU, in which the combination of the first active ingredient (ezetimibe) and the second active ingredient (simvastatin) features an exclusively additive effect as opposed to the straight active ingredients.

The therapeutic effect of ezetimibe consists in inhibiting the intestinal absorption of cholesterol. Purely additively, the combination with simvastatin means that the amount already reduced by ezetimibe, which arrives in the liver, will be broken down more rapidly. This leads to a strengthened reduction of LDL cholesterol. This was also proven by the study shown in the approval procedure for EZETROL®. A dose of 10 mg of simvastatin reduces LDL cholesterol by 27%, while a dose of 10 mg of ezetimibe achieves a reduction of 19%. The effect of the combination preparation with 10 mg each of simvastatin and ezetimibe, which achieves a 46% reduction, is obviously purely additive.

In light of the fact that claim 17 of the Basic Patent names eight statins other than simvastatin, the danger exists, comparably to the Actavis/Sanofi case,

that, besides the combination of ezetimibe with simvastatin, protection certificates would need to be granted for eight more combination preparations, which would be irreconcilable considering the weighing of interests of the pharmaceutical industry and those of the public health (cf. CJEU, GRUR 2014, 157 - Actavis/Sanofi, marg. no. 41). It is not apparent that simvastatin has any more added inventive value than the other statins. This is also confirmed by the statements of the privately obtained expert opinion Assmann (cf. privately obtained expert opinion Assmann dated 24 August 2015, marg. no. 37, Exhibit HL 6a; privately obtained expert opinion Assmann dated 22 May 2018, marg. no. 37, Exhibit HL 18a), according to which the effectiveness of ezetimibe to further reduce the LDL cholesterol level was evident when combined with lovastatin, pravastatin and atorvastatin besides the combination with simvastatin.

(2)

But even if one recognises (along with the Chamber) technical achievements and effects instead of purely synergistic effect, it is not apparent in the case at hand that the reduction of side effects through the combination preparation constitutes the inventive core of the Basic Patent. At no point does the Basic Patent address the fact that the side effects of simvastatin can be avoided by adding ezetimibe, since the amount of simvastatin to be administered can be reduced by the amount of ezetimibe to be administered. It is also untrue that ezetimibe directly counteracts the side effects of simvastatin. Instead, the reduction or avoidance of side effects results from the reduction of the dose of simvastatin by being combined with ezetimibe, and thus is ultimately based only on the additive effect. Neither can this be surmised from the general dosing information in paragraph [0093] (=paragraph [0066]), which corresponds exactly to the dosing of simvastatin as a mono-preparation.

This advantage of avoiding side effects leading to liver damage and rhabdomyolysis, which Injunction Plaintiff argues, cannot be found in the Basic Patent. Injunction Plaintiff itself states that this involves a surprising effect. At no point does the Basic Patent imply that this had already come to light on the priority date so that the person skilled in the art would recognise it as a core of the invention. Instead, what is involved here is additional findings which were not gained until the approval procedure. The sweat-of-the-brow-protection of the supplementary protection certificate, however, benefits the Patentee only for the section

of his invention which he already held in his hands on the priority date. The "sweat" already covered by the supplementary protection certificate is applied to prove the invention with clinical data so that it will be approved for the pharmaceutical market. Additional findings which arise during that procedure are not covered. On the priority date, it was known only that ezetimibe inhibits the absorption of cholesterol and, when combined with the accelerated breakdown through simvastatin, reduces the cholesterol level. According to Injunction Plaintiff's submission, the effective avoidance of side effects which would otherwise arise when statins were administered was unknown in the oral hearing. Instead, the most promising statin (simvastatin) was singled out so it could be aligned with ezetimibe during the approval study. The fact that the statin no longer had to be given in the maximum dose, with the risk of muscle damage, to achieve the desired reduction of LDL cholesterol (cf. privately obtained expert opinion Assmann dated 24 August 2015, Exhibit HL 6a; privately obtained expert opinion Assmann dated 22 May 2018, Exhibit HL 18a), was first proven during later studies of the combined administration of ezetimibe with simvastatin. But this work of Injunction Plaintiff is already covered by Certificate I. And to complicate matters, the relevant studies were already performed for the most part when EZETROL® was approved. The studies described in the technical information for EZETROL® entail the administration of ezetimibe in combination with four statins, including simvastatin (cf. privately obtained expert opinion Dr Lehmann dated 22 June 2018, page 5, Exhibit AG 7 from the parallel proceedings 4b O 40/18). To that end, simvastatin was one of the active ingredients most frequently used in combination (cf. privately obtained expert opinion Dr Lehmann dated 22 June 2018, page 7, Exhibit AG 7 from the parallel proceedings 4b O 40/18). In contrast, regarding the studies for INEGY®, marginally expanded data on effectiveness were submitted at best (cf. privately obtained expert opinion Dr Lehmann dated 22 June 2018, page 9, Exhibit AG 7 from the parallel proceeding 4b O 40/18), which include no findings gained compared to the data from the EZETROL® studies (cf. privately obtained expert opinion Dr Lehmann dated 22 June 2018, page 11, Exhibit AG 7 from the parallel proceedings 4b O 40/18). Injunction Plaintiff has already rightly received Certificate I for EZTROL®.

The fact that the combination is administered in a "fix dose" is revealed in the Basic Patent in claim 9, and in the general dosing information in

paragraphs [0091], [0093] (=paragraphs [0064], [0066]). The person skilled in the art knows due to his general expertise that administration in a standardised pharmaceutical carrier makes taking the drug easier and contributes to improved compliance from patients. It is not recognisable that the manufacturing of the combination in a pharmaceutical carrier has given the person skilled in the art special difficulties which have to be overcome through the Basic Patent. Furthermore, it cannot be inferred from the patent that the improved compliance represents a new therapeutic concept or was a specifically targeted goal.

cc)

The Chamber sees no reason to doubt its results due to the foreign rulings, which have been only partly translated. For one thing, the Chamber is not bound by a foreign ruling which affects other jurisdictions. For another, the rulings do not paint a unified picture. The argumentative approaches are chosen with great variety, and the decisions to dismiss lack the various elements required under Art. 3 SPC Regulation. A unified understanding of the case law of the member states, to which the Chamber would object, cannot be identified at all.

4)

And the weighing of interests which is also called for points the Chamber to no other conclusion. If the injunction certificate was unjustly granted–which the reasons cited seem to indicate more often than not—Injunction Plaintiff is not incurring any damage, but is taking advantage of an unjust monopoly position which it must relinquish. Nevertheless, an additional viewpoint must be included in the weighing of interests which argues for the revocation of the injunction. The legal issue to be decided here is complex, which is true not least because diverse European courts are currently struggling with it and, as already mentioned, are arriving at different conclusions. For one thing, this is related to the fact that judgments of the CJEU have increasingly arrived at different case circumstances in recent years, which are understood consistently differently in European case law and literature. For another, it has to do with the circumstances

of the individual case, which lead to a different constellation of facts than in the cases previously decided. However, the accumulation of a question which has not been cleared up by the case law of the CJEU down to the last detail along with the peculiarities of the individual case means that the principle, which also marks the case law of special cases in Düsseldorf, can no longer be affirmed, so a preliminary injunction comes into question only if an erroneous decision is not seriously expected which would need to be revised later in subsequent proceedings on the merits. In the special case of the generic drug manufacturer established by the Higher Regional Court of Düsseldorf, this requirement has already been fulfilled on the part of the infringing party. In the case at hand, however, the Chamber cannot rule out that a preliminary injunction would not have to be revised, because, for example, one of the many courts seized, may consider again to make a referral to the CJEU.

III.

The non-admitted pleadings of Injunction Defendant dated 18 September 2018 and of Injunction Plaintiff dated 20 September 2018 give no cause to reopen, Sections 296a, 154 ZPO. If nothing else, because the present case is an expedited proceedings.

IV.

The decision on costs is based on Section 91 para. 1 ZPO.

The decision regarding preliminary enforceability is based on Sections 708 no. 6, 711 ZPO.

V.

The value in dispute is assessed at EUR 3,000,000.00.

Dr Voß	Dr Thom	Terlinden
Presiding Judge at the Regional Court	Judge at the Regional Court	Judge at the Regional Court

Certified
Registrar of the Court Regional Court of Düsseldorf