Düsseldorf Higher Regional Court, 2 U 116/22

Date:	February 23, 2023
Court: Panel: Type of decision:	Düsseldorf Higher Regional Court 2nd Civil Senate Judgment
Reference number: ECLI:	2 U 116/22 ECLI:DE:OLGD:2023:0223.2U116.22.00

Previous instance:	Düsseldorf District Court, 4b O 50/22
Guiding Principles:	

Summary of I-2 U 116/22:

1.
The granting of the patent with third party participation does not justify an injunction even in a generic case if it is opposed by the revocation decision of the superior opposition division on the parent patent with the same content.

2
If a previously known dose-finding study (here: for the treatment of multiple sclerosis) discloses, in addition to two ineffective active substance doses (here: 120 mg/day, 360 mg/day), a therapeutically effective dose (here: 720 mg/day), which is associated with comparatively low side effects, the person skilled in the art has reason to test a lower active ingredient dose (480 mg/day), which has not yet been investigated in the study, even if the study has not revealed any evidence that there is a relationship between the amount of active ingredient and the side effects, which would lead to the expectation that a lower level of side effects is associated with a lower amount of active ingredient.

3.

The reason arises from the fact that the study skipped several possible dosage steps (here: 480 mg/day and 600 mg/day) between the ineffective dosage (here: 360 mg/day) and the proven effective dosage (here: 720 mg/day), and it would represent a real stroke of luck if the first and lowest therapeutically effective dose had been found by chance with the active substance dose tested - omitting several possible lower doses - (here: 720 mg/day).

4.
From an expert point of view, the efficacy limit had not yet been determined with the study. To pursue it and to clarify the efficacy limit for its own sake may have been unreasonable from an economic point of view. However, this does not make the project inventive, because the results of the study not only clearly revealed the remaining knowledge gap, but it was also obvious what had to be done to close it.

Tenor:

I. The appeal against the judgment of the 4b Civil Chamber of the Düsseldorf District Court pronounced on September 22, 2022 (file no.: 4b O 50/22) is dismissed.

II. The injunction plaintiff must also bear the costs of the appeal proceedings.

. The amount in dispute for the appeal proceedings is set at € 5,000,000.

R e a s o n s :

I.

The injunction plaintiff, as the registered owner of the German part of the European patent X XXX XXX (hereinafter: injunction patent), asserts a claim for injunctive relief by way of interim legal protection due to its infringement by the pharmaceutical "D" (challenged embodiment), which has been marketed by the injunction defendant, a generic drug company, since May 23, 2022.

The patent for injunction arose from a divisional application of the application underlying the European patent X XXX XXX (hereinafter: parent patent) and claims its filing date of February 7, 2008 as well as the priority of US XXXXXX of February 8, 2007. The notice of grant of the patent-in-suit was published on July 20, 2022 - after objections of third parties were considered in the examination procedure. The patent-in-suit is in force. No decision has yet been made on the opposition to the patent-in-suit filed by the injunction defendant, among others.

Claims 1 and 5 of the patent-in-suit read in German translation as follows:

1. A pharmaceutical composition for use in the treatment of multiple sclerosis, said composition comprising:

(a) dimethyl fumarate or monomethyl fumarate and

(b) one or more pharmaceutically acceptable excipients,

wherein the composition is to be administered orally to a patient in need of treatment for multiple sclerosis and wherein the dose of fumaric acid dimethyl ester or fumaric acid monomethyl ester to be administered is 480 mg per day.

5. Dimethyl fumarate or monomethyl fumarate for use in the treatment of multiple sclerosis, wherein the dimethyl fumarate or monomethyl fumarate is to be administered orally at a dose of 480 mg per day to a patient in need of treatment for multiple sclerosis.

In opposition proceedings conducted by ten opponents - including the injunction defendant - the parent patent was revoked by the Opposition Division of the European Patent Office by decision of June 13, 2016, on the grounds that there was a lack of inventive step, also with regard to the auxiliary requests filed last (written reasons submitted as Exhibit rop 14, in German translation as Exhibit rop 14a; hereinafter cited as "Opposition Decision" after Exhibit rop 14a). The appeal against this decision was rejected by the Technical Board of Appeal in its decision of January 20, 2022 (written reasons submitted as Exhibit rop 10, in German translation as Exhibit rop 10a; hereinafter cited as "Decision TBK" after Exhibit rop 10a) because the subject matter of the auxiliary requests went beyond the content of the application as filed.

Claims 1 and 7 of the parent patent as issued read in German translation as follows, with deviations from the wording of claims 1 and 5 of the patent-in-suit underlined:

1. pharmaceutical composition for use in the treatment of multiple sclerosis, said composition consisting <u>of the following:</u>

(a) dimethyl fumarate or monomethyl fumarate and

(b) one or more pharmaceutically acceptable excipients,

wherein the composition is to be administered orally to a patient in need of treatment for multiple sclerosis and wherein the dose of fumaric acid dimethyl ester or fumaric acid monomethyl ester to be administered is 480 mg per day.

7. Dimethyl fumarate or monomethyl fumarate for use in the treatment of multiple sclerosis, wherein the dimethyl fumarate or monomethyl fumarate is the sole neuroprotective ingredient to be administered, wherein the dimethyl fumarate or monomethyl fumarate is to be administered orally at a dose of 480 mg per day to a patient in need of treatment for multiple sclerosis.

The District Court rejected the injunction plaintiff's request for a preliminary injunction, since the legal validity of the patent for revocation was not secured to the extent required and there was therefore no reason for an injunction. With the decision of the opposition division concerning the parent patent on the one hand and the granting of the patent for injunction on the other hand, relevant decisions of specialized instances were available which were in an irresolvable contradiction to each other. It could be assumed in favor of the injunction plaintiff that a so-called generic case existed, which would require the issuance of a preliminary injunction despite the contradictory decisions, if the Chamber itself could form a sufficient conviction of the legal validity of the patent-in-suit. However, this was not the case.

The injunction plaintiff challenges this with its appeal.

Pursuant to Sections 540 (2), 313a (1) sentence 1, 542 (2) sentence 1 of the Code of Civil Procedure (ZPO), no further description of the facts of the case is provided.

II.

The admissible appeal of the injunction plaintiff is unsuccessful.

The District Court was correct in rejecting the injunction plaintiff's request for a preliminary injunction. The issuance of the requested injunction is not justified because there is no reason for an injunction in view of the fact that the legal situation is not sufficiently secured.

1.

The patent for injunction concerns compositions and their use for the treatment of multiple sclerosis.

Multiple sclerosis (MS), as the patent of disposition describes in its introductory description, is an autoimmune disease in which autoimmune activity is directed against antigens of the central nervous system (CNS). Inflammation in parts of the CNS leads to loss of the myelin sheath around nerve fibers (demyelination), loss of nerve fibers, and eventual death of neurons, oligodenrocytes, and glial cells. MS is a chronic, progressive, disabling disease affecting an estimated 2.5 million people worldwide. It is usually diagnosed between the ages of 20 and 40, although earlier onset is possible. MS is not hereditary, but genetic susceptibility plays a role in its development. Relapsing-remitting MS is manifested by

recurrent relapses with focal or multifocal neurologic disturbances. The relapses can occur seemingly randomly over many years, remitting and recurring. As one attack follows another, because remission is often incomplete, there is gradual deterioration with increasing permanent neurologic deficits.

Various immunotherapeutic drugs can provide relief to MS patients, the patent for injunction continues. However, none of these drugs is able to stop the progression of the disease, and some can cause serious adverse effects. Most current therapies are aimed at reducing inflammation and suppressing or modulating the immune system. Available treatments (as of 2006) reduce inflammation and the number of new relapses, but not all have an impact on disease progression. Some clinical trials have shown that suppression of inflammation in chronic MS rarely limits the accumulation of disability from prolonged disease progression. This suggests that neuronal damage and inflammation are independent pathologies. Some of the most important goals for the treatment of MS are to promote CNS remyelination as a repair mechanism and to prevent axonal loss and neuronal death.

Next, the patent-in-suit explains that "phase 2 enzymes" in mammalian cells serve as a protective mechanism against oxygen/nitrogen species (ROS/RNS), electrophiles, and xenobiotics. Expression of these enzymes, which are not normally expressed at their maximal levels, can be induced by a variety of natural and synthetic agents. Nuclear factor E2-related factor 2 (Nrf2) is a transcription factor responsible for the induction of a variety of important oxidation-inhibiting and detoxifying enzymes.

ROS/RNS are most damaging in the brain and neuronal tissue, where they attack postmitotic (i.e., non-dividing) cells such as glial cells, oligodendocytes, and neurons - which are particularly sensitive to free radicals - resulting in neuronal damage. The dispositive patent describes various observations and prior art findings. These suggest, among other things, that the Nrf2 pathway may be activated as an endogenous protective mechanism in neurodegenerative and neuroinflammatory diseases. It has also been reported that induced activation of Nrf2-dependent genes by certain cyclopenanone-based compounds (NEPP) counteracts the toxic effects of metabolic inhibition of ROS/RNS production in the brain and protects neurons from death in vitro and in vivo. Emerging evidence further suggests that the neuroprotective effects of compounds in natural botanicals, originally attributed to their antioxidant properties, are exerted through activation of cellular stress response pathways, including the Nrf2 pathway, leading to upregulation of neuroprotective genes. However, the exact mechanism of action of these compounds remains poorly understood. To date, more than ten different chemical classes of inducers of the Nrf2 pathway have been identified.

The patent-in-suit acknowledges a publication titled "BG00012, a Novel Oral Fumarate is Effective in Patients with Relapsing Remitting Multiple Sclerosis" by K. et al. which reports the results of a phase II b study reporting the efficacy of three doses (120 mg/day, 360 mg/day, 720 mg/day). It was found, according to the disposition patent, that BG00012 (=

DMF) at a dosage of 720 mg/day (240 mg tid) significantly reduced the activity of MRI-detectable brain lesions in RRMS patients.

The patent-in-suit does not explicitly name a task. However, it can be inferred from paragraphs [0001] and [0010] that the patent-in-suit sees this in the provision of a treatment for MS (cf. opposition decision, p. 31, point 8.1). The Opposition Division sees, as will be explained in more detail, the objective task of the parent patent in providing an alternative daily dose of DMF (or MMF) for the effective oral treatment of MS (cf. Opposition Decision, p. 31, point 8.6.1).

To solve the problem, claim 1 provides a combination of the following features:

1. A pharmaceutical composition for use in the treatment of multiple sclerosis comprising:

1.1. Fumaric acid dimethyl ester or fumaric acid monomethyl ester and

1.2. One or more pharmaceutically acceptable excipients.

2. The composition is to be administered orally to a patient in need of treatment for multiple sclerosis.

3. The dose of fumaric acid dimethyl ester or fumaric acid monomethyl ester to be administered is 480 mg per day.

Claim 5 can be divided into the following features:

1. Fumaric acid dimethyl ester or fumaric acid monomethyl ester for use in the treatment of multiple sclerosis.

2. Fumaric acid dimethyl ester or fumaric acid monomethyl ester is to be administered orally at a dose of 480 mg to a patient in need of treatment for multiple sclerosis.

A composition according to claim 1 of the patent-in-suit thus comprises, in addition to a pharmaceutically acceptable excipient, either dimethyl fumarate (DMF) or monomethyl fumarate (MMF). However, it is not limited to DMF or MMF as the sole active ingredient, but may also contain other active ingredients, as the skilled person would infer from the wording "composition, ... which *comprises"* - in the English procedural language relevant under Art. 70(1) EPC: "composition *comprising".* Claim 5 of the patent-in-suit claims DMF or MMF for use in the treatment of MS, which, in the absence of a limiting specification, also need not be the sole active ingredient. A limitation to DMF or MMF as the only neuroprotectant to be administered is only contained in subclaims 6 to 8 of the patent-in-suit.

On the other hand, claim 1 of the (legally revoked) parent patent is limited to DMF or MMF as the only active ingredient (so-called monotherapy) according to the insofar deviating wording "the composition *consisting of*" in its granted version. Claim 1 of the parent patent thus excludes the presence of other active ingredients in addition to DMF or MMF, e.g. active ingredients suitable for the treatment of MS according to the same or a different

mechanism of action (see decision TBK, p. 9, point 4.1). The same applies to claim 7 of the parent patent, which is also limited to DMF or MMF as the only neuroprotectant to be administered.

There are no further differences between claims 1 and 5 of the patent-in-suit on the one hand and claims 1 and 7 of the parent patent on the other hand, as the parties rightly agree.

2.

The necessary reason for an injunction is lacking, because the legal existence of the patent in suit is not secured to the extent required for the issuance of a preliminary injunction.

a)

It corresponds to the consistent case law of the Senate (InstGE 9, 140 - Olanzapin; InstGE 12, 114 - Harnkatheterset; GRUR-RR 2011, 81, 82 - Gleitsattel-Scheibenbremse II; Judgment ofDec. 06, 2012, file no.: I-2 U 46/12, BeckRS 2013, 13744; GRUR-RR 2013, 236, 239 f. - Flupirtin-Maleat; file no. Nov. 07, 2013, file no.: I-2 U 94/12, GRUR-RS 2014, 04902 - Desogestrel; judgment v. Dec. 18, 2015, file no.: I-2 U 35/15, GRUR-RS 2016, 6208 para. 18 - diagnostic procedure; Judgment ofAug. 31, 2017, file no.: I-2 U 11/17, BeckRS 2017, 125974 para. 48; judgment of. Dec. 14, 2017, file no.: I-2 U 18/17, GRUR-RS 2017, 142305 para. 12 - combination composition; judgment of. Sept. 26, 2019, file no.: I-2 U 28/19, GRUR-RS 2019, 33227 = GRUR-RR 2020, 240 [Ls.] - MS-Therapie; GRUR-RR 2021, 249, 250 - Cinacalcet II; GRUR-RR 2021, 400, 402 - MS-Therapie II) that the issuance of a preliminary injunction, in particular for injunctive relief, can only be considered if both the question of patent infringement and the existence of the right to injunctive relief can be answered so clearly in favor of the injunction plaintiff that an erroneous decision to be revised in any subsequent main proceedings is not to be seriously expected. This can be assumed - in view of the persistently high revocation and cancellation rate of granted patents, according to which out of 10 IP rights challenged with an opposition or nullity action only about 3 prove to be legally valid in the granted scope (cf. the evidence in Kühnen, Handbuch der Patentverletzung, 15th ed, Chap. G para. 57) - can regularly only be assumed if the patent-in-suit has already survived opposition or nullity proceedings in the first instance (Senate, InstGE 9, 140, 146 - Olanzapin; InstGE 12, 114 - Harnkatheterset; GRUR-RR 2011, 81, 82 - Gleitsattel-Scheibenbremse II; Judgment of07.11.2013, file no.: I-2 U 94/12, GRUR-RS 2014, 04902 - Desogestrel; Judgment ofDec. 18, 2014, file no.: I-2 U 60/14, BeckRS 2015, 01829 para. 17; judgment of. Dec. 18, 2015, file no.: I-2 U 35/15, GRUR-RS 2016, 6208 para. 18 - diagnostic procedure; Judgment ofAug. 31, 2017, file no.: I-2 U 11/17, BeckRS 2017, 125974 para. 48; judgment of. Dec. 14, 2017, file no.: I-2 U 18/17, GRUR-RS 2017, 142305 para. 12 - combination composition; judgment of. Sept. 26, 2019, file no.: I-2 U 28/19, GRUR-RS 2019, 33227 = GRUR-RR 2020, 240 [Ls.] - MS-Therapie; GRUR-RR 2021, 249, 250 - Cinacalcet II GRUR-RR 2021, 400, 402 - MS-Therapie II). Therefore, in order to make an injunction suitable for preliminary injunction proceedings anticipating the main action, a positive decision by the competent opposition or nullity courts equipped with technical expertise is generally required.

Whether the admissibility of this practice has changed as a result of the decision of the ECJ in Case C-44/21 (GRUR 2022, 811 - Phoenix Contact/Harting) (see Kühnen, loc. cit, para. 81 et seq.; Deichfuß, GRUR 2022, 800; Keßler/Palzer, EuZW 2022, 562; Stierle, Mitt 2022, 277), does not need to be decided in the case in dispute, because the issuance of a temporary injunction - as will be explained below - is prohibited in the present case without taking into account any precedence of an expert decision on the validity of the patent for injunction.

According to the established case law of the Senate, the requirement of an adversarial decision favorable to the plaintiff may be waived in special cases. This applies, for example, if the injunction defendant (or another serious competitor) has already participated in the grant proceedings with his own objections, so that the grant of the patent is factually equivalent to the decision in a two-sided opposition proceeding, if a decision on the existence of rights has therefore not been made, because the right of disposal is generally recognized as being protectable (which is reflected by the existence of well-known licensees or the like), if the objections to the legal validity of the right of disposal already prove to be groundless in the summary examination peculiar to preliminary legal protection proceedings, or if (e.g., in view of the market situation) the right of disposal is generally recognized as being protectable (which is reflected by the existence of well-known licensees or the like). or if (e.g., with regard to the market situation or the disadvantages threatening from the infringement of the property right) there are exceptional circumstances which make it unreasonable for the plaintiff for an injunction to wait for the outcome of the opposition or nullity proceedings (cf. Senat, InstGE 12, 114, 121 - Harnkatheterset; Judgment of07.11.2013, Az.: I-2 U 94/12, GRUR-RS 2014, 04902 - Desogestrel; GRUR-RR 2013, 236, 240 - Flupirtin-Maleat; Judgment of Dec. 18, 2015, file no.: I-2 U 35/15, GRUR-RS 2016, 6208 para. 19 – diagnostisches Verfahren; judgment of. Dec. 14, 2017, file no.: I-2 U 18/17, GRUR-RS 2017, 142305 para. 12 - Kombinationszusammensetzung).

Such a situation regularly arises in the case of infringing acts by generic companies. While the damage caused by them in the case of a later maintenance of the patent is often enormous and (with regard to the price decline caused by a corresponding fixing of reference prices) irreparable, an unjustified injunction (due to a later destruction of the patent) only has the consequence that the generic company is temporarily wrongfully kept away from the market, which can be fully compensated by corresponding claims for damages against the patent owner. It must also be taken into account that the generic drug company generally does not incur any economic risks of its own for its market presence (because the preparation is sufficiently medically tested and established on the market thanks to the patent owner). For this reason, a prohibition order must be issued even if the infringement court, in the absence of an expert decision on the legal status, cannot obtain final and unambiguous certainty on the legal status, provided that the infringement court (on the basis of its own assessment, which is possible for it in view of the technical matter concerned) is convinced (in the sense of sufficient prima facie evidence) that the injunction is legally valid, because it will not be possible to establish the lack of patentability of its subject matter of invention. For this, from the point of view of the infringement court, either the better arguments must speak in favor of patentability, so that this can be positively affirmed, or the question of patentability must at least remain unclarified (with regard to the distribution of the burden of proof applicable in the proceedings on the existence of rights), so that the infringement court, if it had to decide on the matter itself instead of the Patent Office or the BPatG, would have to affirm its existence of rights (Senat, GRUR-RR 2013, 236, 240 - Flupirtin-Maleat; Judgment of November 7, 2013,

File no.: I-2 U 94/23, GRUR-RS 2014, 04902 - Desogestrel; Judgment of Feb. 19, 2016, file no.: I-2 U 54/15, BeckRS 2016, 6344 para. 13; judgment of. 14.12.2017; Judgment of Dec. 14, 2017, file no.: I-2 U 18/17, GRUR-RS 2017, 142305 para. 12 - Combination composition; GRUR-RR 2021, 249, 252 - Cinacalcet II; GRUR-RR 2021, 400, 403 - MS-Therapie II).

Conversely, it also follows from the regular necessity of a positive disputed decision on the existence of the law that, as soon as it is available, it must in principle be assumed that the existence of the patent-in-suit is sufficiently secured (Senate, Judgment of 19.02.2016, file no.: I-2 U 54/15, BeckRS 2016, 6344 para. 12; judgement of. Dec. 14, 2017, file no.: I-2 U 18/17, GRUR-RS 2017, 142305 para. 12 - Combination composition; judgment of. Sept. 26, 2019, file no.: I-2 U 28/19, GRUR-RS 2019, 33227 = GRUR-RR 2020, 240 [Ls.] - MS-Therapie; GRUR-RR 2021, 249, 251 - Cinacalcet II). The infringement court - irrespective of its duty to seriously examine the prospects of success of the attacks directed against it even after the conclusion of the first instance proceedings in order to form a picture of the protectability of the invention on its own responsibility - must in principle take into account the technical and scientific information provided by the competent technical authority (DPMA, EPO, BPatG) after a technically competent examination and, unless there are special circumstances in the individual case, to draw the necessary conclusions by issuing the required cease-and-desist orders for the protection of the patent owner (Senate, Judgment of19.02.2016, file no.: I-2 U 54/15, BeckRS 2016, 6344 para. 12; Judgment of14.12.2017; Judgment of Sept. 26, 2019, file no.: I-2 U 28/19, GRUR-RS 2019, 33227 = GRUR-RR 2020, 240 [Ls.] - MS-Therapie; GRUR-RR 2021, 249, 251 - Cinacalcet II). Reason to doubt the decision as to the existence of the law and to refrain from an injunction only exists if the infringement court considers the argumentation of the opposition or nullity instance to be unreasonable or if the attack on the patent-in-suit undertaken with the appeal against the opposition or nullity decision is based on (e. g.(e.g., new) promising aspects that have not yet been taken into account and decided by the bodies that have dealt with the matter so far (Senate, judgment of December 6, 2012, file no.: I-2 U 46/12, BeckRS 2013, 13744; GRUR-RR 2021, 249, 251 f. - Cinacalcet II). In contrast, as a rule, it is not appropriate to reject the application for an injunction despite the property right being upheld in the first instance solely because the infringement court substitutes its own (lay) assessment of the technical facts for the assessment by the competent opposition or nullity instance (Senate, Judgment of Dec. 18, 2014, file no.: I-2 U 60/14, BeckRS 2015, 01829 para. 17; judgment of. 19.02.2016, file no.: I-2 U 54/15, BeckRS 2016, 6344 para. 12; judgment of. Dec. 14, 2017; GRUR-RR 2021, 249, 252 - Cinacalcet II). This is particularly prohibited if the subject matter is technically complex (e.g. from the field of chemistry or electronics), with regard to which the insights and assessment possibilities of the technically untrained infringement court are limited from the outset.

Responsible use of the means of an injunction, which in case of doubt places a lasting burden on the respondent, also requires - conversely - that the existence of a negative disputed decision on the existence of the law generally precludes the assumption of a secure existence of the law. Thus, the reason for an injunction must generally be negated if a first instance decision has been issued which has revoked the patent or declared it invalid (Senate, InstGE 9, 140 - Olanzapin; InstGE 12, 114 - Harnkatheterset; Judgment of Aug. 31, 2017, file no.: I-2 U 11/17, BeckRS 2017, 125974 para. 50). Even if a preliminary decision holds out the prospect of the destruction or a restriction

of the patent-in-suit leading out of use, the infringement court will not be able to form a conviction of the legal status in case of doubt due to the lack of superior technical expertise of its own (Senate, GRUR-RR 2021, 249, 252 et seq. - Cinacalcet II; judgment of March 4, 2021, file no.: I-2 U 32/20, GRUR-RS 2021, 4506 para. 10 - Cinacalcet III; cf. also judgment of Sept. 26, 2019, file no.: I-2 U 28/19, GRUR-RS 2019, 33227 para. 52 = GRUR-RR 2020, 240 [Ls.] - MS-Therapie). This applies in the same way in the case of a decision on the existence of a right relating to a parent or parallel patent if its argumentation leading to the destruction of the property right can be transferred to the right of protection against injunction (cf. Senate, judgment of. 26.09.2019, file no.: I-2 U 28/19, GRUR-RS 2019, 33227 para. 52 = GRUR-RR 2020, 240 [Ls.] - MS-Therapie).

b)

On this basis, the legal existence of the patent-in-suit is not secured to the extent sufficient for the issuance of a preliminary injunction.

aa)

First of all, it must be stated that a constellation exists in which the requirement of a positive disputed decision on the existence of the law can be dispensed with according to the standards described. This is because the decision on the grant of the patent-in-suit was - (1) - made with the participation of third parties and - (2) - irrespective of the fact that the challenged embodiment was already on the market at the time of the grant of the patent-in-suit ,it is a generic case within the meaning of the principles outlined above. Both aspects suspend the requirement of a positive disputed legal status decision.

However, the decision of the Opposition Division of the European Patent Office to revoke the parent patent, which is largely identical in content to the patent in suit and even narrower in scope due to the limitation of the active ingredient, precludes the issuance of a preliminary injunction, which leads to the expectation that the patent in suit will also prove to be unenforceable in the ongoing opposition proceedings.

Compared to the Examining Division, the Opposition Division is a higher-ranking body of appeal, which is why the decisions of two bodies of appeal of at least equal rank do not confront each other (equivalently). Rather, the decision of the opposition division on the parent patent is a negative decision on the legal status of the patent issued in adversarial proceedings by a technically competent board of appeal, which - provided that it is transferable to the patent for revocation and is not called into question by the subsequent decision of the Technical Board of Appeal - regularly excludes the assumption of a secure legal status. Under these conditions, there is no reason to question the decision of the opposition division if, instead of the argumentation of the decision on the legal status, other conclusions and thus a different decision would be possible with equally or at least also justifiable considerations, but only if the Senate considers the argumentation not justifiable or if (e.g. new) promising aspects are raised against

the opposition to the patent-in-suit which the opposition division has not yet considered and decided. This applies irrespective of whether the opposition division dealing with the patent for revocation will decide in the same composition of staff that decided on the opposition against the parent patent.

A different view is not required because, exceptionally, particular weight would have to be attached to the grant of the patent-in-suit. In this respect, the injunction plaintiff relies on the fact that the grant of the patent-in-suit - which took place six years after the decision of the Opposition Division and with the participation of one of its members as examiner - was made on the basis of detailed oral proceedings and taking into account both the decision of the Opposition Division and the submissions made in the meantime by all parties, including itself. Treating the grant of the patent-in-suit on these grounds as equivalent to the decision of the Opposition Division is not possible, because nothing is known about the content of the non-public oral proceedings or about the considerations of the Examining Division on which the grant of the patent-in-suit was based. In a communication of the Examining Division from June 2022 (Exhibit rop 13), it merely states in a very general way:

"The arguments provided in the TIPAs in relation to Art. 56 EPC relate to the parent application. The present divisional application is a new application, independent from the parent. The arguments provided by the OD in relation to the parent have been considered and found that are not applicable to the present divisional."

In German translation:

„*Die in den Einwendungen Dritter (TIPAs) vorgebrachten Argumente in Bezug auf Art. 56 54 ER) beziehen sich auf die Stammanmeldung. Die vorliegende Teilanmeldung ist eine neue Anmeldung, unabhängig von der Stammanmeldung. Die von der Einspruchsabteilung in Bezug auf die Stammanmeldung vorgebrachten Argumente wurden berücksichtigt und als auf die vorliegende Teilanmeldung nicht anwendbar befunden."*

To what extent the examining division took into account the facts available to it and for what precise reasons (contrary to the considerations of the opposition decision) it came to the conclusion that the arguments relating to the parent application were "not applicable" to the divisional application from which the patent-in-suit arose, cannot be inferred from this. To the extent that the injunction plaintiff merely states in a general manner and without further substantiation that it had convinced the Examining Division with its arguments in the grant proceedings for the patent for revocation that the decision of the Opposition Division was not only outdated but also wrong, this view is in any case not reflected in the brief communication of the Examining Division. Moreover, the factual submissions of the injunction plaintiff do not provide any specific information as to the arguments on the basis of which the conclusions of the opposition division were deemed to be unsustainable when granting the patent-in-suit. Should the examining division not have made any statement on this to the parties, the injunction plaintiff would not have to be accused of a lack of substantive argument; however, for the Senate it would remain the case that the opposition decision must in principle be given greater weight due to the superior position of the examining division in the appeal proceedings and that it must remain so until it is concretely comprehensible on the basis of which considerations the examining division did not follow it. Only when there is clarity in this

respect would the Senate be in a position to understand whether the Examining Division's divergent view is convincing to such an extent that it must - exceptionally - be given precedence over the opposition decision, because it is likely that the Opposition Division will not be able to ignore the Examining Division's assessment in its future decision on the legal validity of the patent-in-suit.

Nor can a special significance of the act of granting be derived from the partial identity of the personnel of the examination and opposition divisions. The priority of the opposition decision is not based on the superior expertise of the individuals who made the decision, but on the organizational superiority of the decision-making body in the chain of instances.

Insofar as the injunction plaintiff relies on a presumption of the validity of the patent in suit to be derived from the decision of the ECJ in Case C-44/21 (GRUR 2022, 811 - Phoenix Contact/Harting), nothing else follows from this either. Even if such a presumption existed, it would be refuted by the final revocation of the parent patent and, moreover, it would not lead to the grant decision, which was issued without documented reasons, being equal in rank and significance to the detailed considerations of the opposition division or even being preferred. Further comments on possible conclusions to be drawn from the above-mentioned decision are unnecessary, since, as described, a constellation exists in which the requirement of an adversarial decision on the legal status of the patent is to be dispensed with in any case according to the Senate case law described above.

bb)

Having said this, the decision of the Opposition Division on the parent patent is contrary to the assumption of a secure legal existence of the patent-in-suit. This is because it is transferable to the patent for revocation, is not called into question by the subsequent decision of the Technical Board of Appeal and, moreover, does not appear to be unjustifiable for reasons which the Senate itself can determine, nor are (e.g. new) promising aspects raised against the opposition to the patent for revocation which the Opposition Division did not consider and decide. Furthermore, from its - necessarily technically lay - point of view, the Senate considers the considerations of the opposition division not merely justifiable, but convincing in substance, and would therefore take the same decision as the opposition division on the parent patent if it had to decide on the validity of the patent for revocation. The Senate therefore shares the opinion of the District Court that the patent-in-suit is unlikely to survive the pending opposition proceedings.

(1)

The fact that the considerations of the Opposition Division are transferable to the teaching of the patent in suit is also rightly not disputed by the injunction plaintiff. The only difference between claims 1 and 5 of the patent-in-suit and claims 1 and 7 of the parent patent, as discussed, is that the parent patent is limited to DMF or MMF as an active ingredient or neuroprotectant, whereas

the patent-in-suit allows the presence of other active ingredients. The revoked parent patent is thus even narrower in scope than the patent-in-suit, and the prior art cited in opposition to the patent-in-suit is therefore a fortiori applicable to the patent-in-suit .

(2)

The decision of the Opposition Division is not called into question by the subsequent decision of the Technical Board of Appeal. It is true that the Technical Board of Appeal did not examine the ground for revocation of lack of inventive step assumed by the Opposition Division, but dismissed the appeal on a different ground - inadmissible broadening (Article 123(2) EPC). However, this does not indicate that the opposition division's assessment was incorrect from the point of view of the Technical Board of Appeal. As the District Court also pointed out, the inadmissible extension is an independent ground for opposition leading to revocation (Art. 101, para. 1, sentence 1, Art. 100(c) EPC), which logically has priority in principle (because the question of novelty and inventive step can only be meaningfully raised and answered with a view to a legally admissible version of the claim) and the existence of which makes further explanations unnecessary. Accordingly, the question of inventive step was not discussed in the oral proceedings before the Technical Board of Appeal, as the injunction plaintiff has submitted without contradiction.

Whether, conversely, the decision of the Technical Board of Appeal contains indications that the reason for revocation of the inadmissible extension could also be relevant for the patent-in-suit can be left open - since the inadmissible extension is partly justified by the restriction of the parent patent to DMF or MMF as the only active ingredient and the explanations can thus in any case not be transferred in their entirety.

(3)

Also in view of the objections of the injunction plaintiff, the Senate is not able to establish that the assessment of the Opposition Division is not justifiable, which with regard to the parent patent - based on the presentation "Efficacy of a novel single-agent Fumarate, BG00012, in patients with relapsing-remitting multiple sclerosis: results of a phase II study" by K. et al. (citation D11-A3; submitted as Exhibit AG1_D4; hereinafter: K.) - denied inventive step (Art. 56 EPC).

Applying the so-called task-solution approach, the opposition division determined the closest prior art, then determined the task to be solved in the light of this teaching, and finally examined the question of whether the claimed invention was obvious to the skilled person in view of this. In doing so, the Opposition Division determined K. as the closest prior art and found that the difference between the teaching of the parent patent and K. was the lower daily dose claimed in the parent patent (namely 480 mg/day versus 720 mg/day). On this basis, the Opposition Division stated, inter alia, that the surprising effect of a dosage of 480 mg/day compared to 720 mg/day, as claimed by the patent proprietor and injunction plaintiff here, had to be disregarded in the definition of the objective technical task because

this effect could not be derived from the application as filed and the post-publication evidence submitted by the injunction plaintiff therefore had to be disregarded. On this basis, the objective technical task was not to provide an improved or optimized dosage regimen for the effective oral treatment of MS, but was to be formulated as providing an *alternative* daily dose of DMF for the effective oral treatment of MS. Faced with the task thus formulated, the skilled person, according to the opposition division, would arrive at the solution of the claims starting from K. alone or in combination with the general expertise represented by D 25 (ICH Topic E 4 "Dose Response Information to Support Drug Registration," November 1994, submitted in English as Exhibit rop 17-D12; hereinafter also: ICH Guidelines).

The assessment of the opposition division derived in this way is neither based on unreasonable considerations nor does a different legal standard of examination to be applied in opposition proceedings against the patent-in-suit lead to the expectation of a different legal result.

(a)

First of all, it cannot be seen that the opposition division made mistakes in defining the objective technical task. In particular, the opposition division gave detailed and comprehensible reasons why, when formulating the task, it did not take into account the surprising effect of a dosage of 480 mg/day claimed by the injunction plaintiff, which can only be derived from post-published evidence.

(aa)

The Opposition Division considered that the application as filed (submitted as Exhibit rop 11, in German translation as Exhibit rop 11a) does not plausibly represent that the specific dose of 480 mg/day of DMF or MMF as the (only) active ingredient solves the task of effectively treating MS. In doing so, it considered the passages of the application under consideration and stated that the only passage dealing with oral administration of DMF in humans does mention various potentially effective doses (cf. para. [0116] of Exhibit rop 11a: "0.1 g to 1 g per day, from 200 mg to 800 mg per day, from 240 mg to 720 mg per day, or from 480 mg to 720 mg per day or 720 mg per day"), none of them could be considered as a plausible solution for inducing an unexpected or surprising technical effect. Errors in this assessment are not apparent.

In the opinion of the Senate, the application as filed - including its claims - also does not contain any other passages which emphasize a dosage of 480 mg/day DMF or MMF as (preferably) effective. On the contrary, the Technical Board of Appeal also stated in its decision on the parent patent that the dose of 480 mg/day does not stand out from the multitude of ranges (cf. decision TBK, p. 11, point 4.2). Admittedly, the question discussed there in the context of the inadmissible extension is whether the dose of 480 mg/day is indicated as a preferred dose or is the result of a selection, which is why the remarks cannot be directly transferred to the plausibility discussed by the opposition division. However, it can be stated in any case that the Technical Board of Appeal

expressly disagrees with the view asserted by the appellant and injunction plaintiff here that the skilled person recognizes the value of 480 mg as known to be effective on the basis of the representation in para. [0116] (Decision TBK, p. 12, para. 4.2.2).

(bb)

It can be left open whether the standard of a so-called ab-initio plausibility applied by the Opposition Division when examining inventive step, which at least at the time of the decision was frequently applied in the case law of the Opposition Divisions and Boards of Appeal of the European Patent Office (cf. the presentation in the decision of the Board of Appeal on the referral to the Enlarged Board of Appeal, file no.: T 0116/18, p. 26 et seq, submitted as Exhibit rop 15, in German translation as Exhibit rop 15a), requires a correction in view of the notice of the Enlarged Board of Appeal of 13.10.2022 submitted by the injunction plaintiff in case G 2/21 (Exhibit rop 29, in German translation as rop 29 a; hereinafter cited as "Notice GB/EPO" after Exhibit rop 29a). Even if this should be the case - which is completely uncertain at present - no other result results for the assessment of the patent-in-suit and its legal existence.

To the extent that the Enlarged Board of Appeal states, with respect to Question 1, that the principle of free assessment of evidence does not appear to permit disregarding evidence per se to the extent that it is submitted and relied upon by a party in support of a contested conclusion relevant to the final decision (GB/EPA Note, p. 3 para. 12), this view is consistent with the Opposition Division's reasoning. As noted above, the Opposition Division did not per se disallow the post-publication evidence relied on by the injunction plaintiff, but provided detailed reasons for its disallowance based on the disclosure in the parent application.

On the other hand, the Enlarged Board of Appeal, in its preliminary legal opinion on questions 2 and 3, appears to allow the consideration of subsequently published evidence under different conditions than those on which the Opposition Division's statements - at least in part - are based. For the Senate, however, it is not convincing that the Opposition Division - had it proceeded from the standard there - would have had to come to the conclusion that the post-published evidence of the injunction plaintiff is to be taken into account and that, based on this, the objective technical task would have had to be determined differently.

The Enlarged Board of Appeal bases its explanations on the fact that the core issue is what the person skilled in the art - taking into account his general technical knowledge - takes as the technical teaching of the claimed invention on the filing date of the application as originally filed. The technical effect claimed must also be encompassed by this technical teaching at a later stage and must embody the same invention (GB/EPA Note, p. 3 para. 15). On the basis of the application documents and the technical teaching disclosed here, an asserted technical effect used for the reasons of the inventive step must then be assessed as to whether the person skilled in the art would have had substantial reason to doubt it (the asserted technical effect relevant to the invention) in view of the general knowledge of the art. If there are no such doubts, according to the preliminary legal opinion of the Enlarged Board of Appeal, recourse to post-published (e.g. experimental) data seems to serve as a possible source for the claimed technical effect in order to decide whether it is convinced of this technical effect or not when deciding on the inventive step of the claimed subject-

matter. In contrast, according to the comment of the Enlarged Board of Appeal, it appears questionable whether such evidence can be successfully relied upon even if the skilled person has considerable doubts about the claimed technical effect on the basis of the application as originally filed and the general knowledge of the art (GB/EPA comment, p. 4, para. 16-18).

Applying this standard, the Opposition Division would therefore have had to first examine what the skilled person would take from the original application as the technical teaching of the claimed invention. Finally, according to the preliminary view of the Enlarged Board of Appeal, the claimed technical effect must also be encompassed by this technical teaching at a later stage and embody the same invention. Already at this point, the Senate is unable to establish that the Opposition Division, taking into account the overall content of the original application, would have come to the conclusion that the technical teaching of the invention is directed to the provision of an effective - possibly lower - dosage of DMF or MMF. The parent application deals with possible dosages for oral administration of DMF or MMF to humans in only one place, namely in paragraph [0116]. According to the presentation there, however, the dosage is permitted within a wide range and left to the individual case, when it is stated (emphasis added):

"For DMF or MMF, an effective amount may range from 1 mg/kg to 50 mg/kg (e.g., from 2.5 mg/kg to 20 mg/kg or from 2.5 mg/kg to 15 mg/kg). Effective dosages also vary, as those skilled in the art know, depending on the route of administration, the use of drug carriers, and the possibility of concomitant use with other therapeutic treatments, including the use of other therapeutic agents. For example, an effective dose of DMF or MMR [sic] to be administered orally to a patient may be from about 0.1 g to 1 g per day, 200 mg to about 800 mg per day (e.g., from about 240 mg to about 720 mg per day; or from about 480 mg to about 720 mg per day; or about 720 mg per day). ..."

The impression of a largely arbitrary dosing of DMF and MMF is additionally strengthened by the immediately following reference in paragraph [0117], where it is stated:

"The dosage (note: as specified in subsection [0116]) *may be determined by a physician and adjusted as necessary to match the observed effects of the treatment. ..."*

However, even if one sees this differently, there is - as far as an assessment is possible for the Senate - no claim of a technical effect directed to the dosage of 480 mg/day in the original application. In view of the breadth of the ranges of possible dosages mentioned in paragraph [0116] - completely indiscriminately and without any preference - with daily doses between 0.1 g (= 100 mg) and 1 g (= 1000 mg), the person skilled in the art does not infer from the descriptive text any concrete assertion of a (superior or even equal) efficacy of certain dosages mentioned there, a fortiori no such assertion of efficacy for a daily dose of 480 mg. Contrary to what the injunction plaintiff claims, paragraph [0116] of the application for registration does not present the specifically mentioned dosages within the range opened up by the introductory wording as somehow advantageous and therefore preferred variants of execution, but rather as examples of a therapeutically effective dose that merely rank equally among each other.

Should this also be seen differently, the Senate considers it likely that the skilled person would have had considerable reason to doubt the claimed efficacy of a single value not emphasized in any way in the descriptive text, based on the standard presented in the note of the Enlarged Board of Appeal.

Several passages in the decision of the opposition division quoted below also indicate that, although it was based on a different standard, it was nevertheless based on a comparable view in the result (emphasis added in each case):

With regard to the aforementioned paragraph [0116], the Opposition Division states (p. 32, para. 8.5):

"Although the application as filed contains information that the 480 mg/day dose may be an effective oral dose of DMF or MMF, it does not disclose the fact that the task was effectively accomplished with the 480 mg/day oral dosage."

In order to distinguish it from the decision T 1642/07 cited by the patent proprietor and injunction plaintiff here, the decision of the Opposition Division states (p. 33, para. 8.6.3):

"P cited, inter alia, T 1642/07 as a basis for accepting post-published evidence to confirm an effect announced in the application. The present case differs from T 1642/07 in that none of the effects were announced in the present case. ..."

With respect to the claimed surprising effect of the 480 mg/day dose, it states (p. 32, para. 8.5 at end):

"As a result, and applying the criteria from the case law book ... the subsequently claimed surprising effect of 480 mg/day versus 720 mg/day DMF cannot be taken into account in the formulation of the objective technical task, since this effect cannot be inferred from the application as filed ."

(b)

However, even if one assumes that the Opposition Division, using the standard stated in the note of the Enlarged Board of Appeal, would have come to the conclusion, based on the consideration of post-published evidence, that the objective technical task was to provide an improved or optimized dosage regimen for the effective oral treatment of MS (cf. Opposition Decision, p. 32, para. 8.6), the Senate is unable to see that this would have led to a result other than the lack of legal existence. This is because the opposition division states that, in view of the side effects associated with the daily dose of 720 mg presented as effective in K.'s slides, the expert had sufficient motivation to optimize the dosage regimen by routine trials (p. 33, para. 8.7.1). On this basis, he would have arrived at the 480 mg/day dosage in the obvious way either using K as a general framework for further dose optimization studies (p. 33, para. 8.7.1 at the end) or using the ICH guidelines according to D 25, which reflect the standard steps of dose optimization (p. 34, para. 8.7.2). The Senate is unable to recognize that and to what extent this assessment would have changed in the case of the

differently determined technical task, as described. Moreover, the Senate considers the explanations with which the opposition division came to the conclusion that the skilled person would have arrived at the teaching of the parent patent in an obvious manner, starting from K., to be comprehensible and convincing.

(aa)

In its reasons, the opposition division assumes that K.'s slides provide sufficient motivation for the expert to optimize the dosage regimen by routine tests, because from them a clearly proven efficacy can be derived only for *one* daily dose (namely 720 mg/day), but this dose is associated with side effects in the gastrointestinal tract.

Irrespective of the question discussed in detail between the parties with the submission of private expert opinions, whether a (possibly statistically relevant) dose dependence of the side effects can be inferred from K.'s slides or whether a dose dependence of the side effects of DMF or MMF was general expert knowledge at the priority date, it cannot be established in any case that the opposition division inappropriately inferred a dose dependence of the side effects from K.'s slides and drew incorrect conclusions on this basis. Rather, the decision of the opposition division only mentions that the daily dose of 720 mg/day is associated with side effects (opposition decision, p. 33, item 8.7.1; cf. also p. 31, item 8.2). The Opposition Division does not make the comparison made by the parties and by the District Court of the side effects at the different dosages examined in the study on which K.'s slides were based. As far as it is stated in the affidavit of Prof. K. submitted by the injunction plaintiff (Exhibit rop 25, there p. 2, item 2.1) that it is clear from item 8.7.1 of the opposition decision that there is a dose-dependent effect with regard to undesired side effects and that this is a motivation for the reduction of the dose of 720 mg/day, this assessment is not substantiated in more detail. On this basis, the Senate is unable to recognize an erroneous interpretation of the side effect profile presented in the slides by K. and an unreasonable assessment of the motivation of the expert based on this.

That the conclusions of the injunction plaintiff would be unjustifiable, the Senate can also not recognize with regard to the further arguments put forward by the injunction plaintiff, according to which the expert would not have had a sufficient expectation of success with regard to a reduction of the dose on the basis of the slides of K. and would have refrained from a renewed dose-finding study - at least in the direction of a reduction of the dose - in view of the available well-tolerated treatment at a dose of 720 mg/day. On the contrary, the considerations of the opposition division appear comprehensible and - at least from a lay pharmaceutical point of view, of which the Senate alone is in a position - plausible.

It must be taken into account that the question of what the person skilled in the art would have taken from the results of the study presented in the K. slides on the priority date and whether he would have carried out further investigations on this basis is to a particular extent not subject to review by the Senate. For while in the case of complex technical subject matter an infringement court can form at least a reasonably well-founded picture of its own, if necessary, to the extent that it is a question of whether the subject matter of the patent-in-suit was disclosed unambiguously and directly in the underlying original application and whether the novelty question can possibly still be surveyed reasonably independently, the decision as to whether the person skilled in the art could.

have arrived at the invention from the prior art in an obvious manner depends on a profound technical understanding and insight into the technical knowledge, the skills as well as the way of thinking and proceeding of an average person skilled in the art at the priority date. As a rule, even an experienced infringement court does not have any expertise of its own in this respect, at least if the inventions involved are not simply mechanical but - as in this case - complex (e.g. pharmaceutical or communications technology). On the other hand, it is the daily task of opposition divisions, boards of appeal and invalidity senates to consider, in the narrow technical field assigned to them in each case, what prior knowledge the relevant skilled person possessed at the relevant time, with what horizon of knowledge he therefore perceived the prior art and with what strategy he attempted to develop it further. Due to their constant and, in case of doubt, long-standing involvement with precisely these questions, the adjudicating bodies of the courts with jurisdiction have a wealth of experience which places the handling of the criterion of inventive step on a legally secure basis. Against this background alone, it is forbidden for an infringement court, which has neither approximately comparable knowledge nor experience with regard to the development work of technicians, to place its own, necessarily entirely lay assessment above the considerations of a well-founded opposition decision. Reason to disregard a decision based on expert reasoning only exists if the body of law is shown to have interpretations or conclusions that are objectively demonstrably incorrect and deprive its assessment of a basis (see already Senate, GRUR-RR 2021, 249, 256 - Cinacalcet II).

The latter cannot be established even taking into account the objections of the injunction plaintiff, in particular the affidavit of Prof. K. (Exhibit rop 25). Admittedly, Prof. K. reaches different results than the opposition division with regard to the question of what the expert would have taken from the slides on the priority date and what steps he would have taken on this basis. For example, Prof. K. states, among other things, that on the basis of the study it could have been expected that a lower dose than 720 mg/day would lead to a lower efficacy (Exhibit rop 25, p. 4, para. 3.3) and that the expert would not perform a dose optimization by lowering the only effective dose according to the phase 2b study (Exhibit rop 25, p. 4, para. 4.2). It has to be conceded that the statements of Prof. K. as one of the leaders of the study assessed in the slides have weight and, as the District Court also saw it, in principle indications for the expert understanding on the priority date can be taken from them. However, the statements of Prof. K. are not impartial statements, but qualified factual statements of the injunction plaintiff, who naturally has an interest in a different assessment of the study results. For this reason alone, the party expert's comments cannot have the same significance for the Senate, which - as stated - lacks well-founded technical expertise in the complex field in question, in assessing the prospects of success of the patent on revocation as is accorded to the thoroughly reasoned decision of the personally and factually independent opposition division. This is all the more true since Prof. K. himself expressly states in his affidavit (Exhibit rop 25, p. 1, item 1.4) that he had already made three statements in the opposition proceedings against the parent patent. In any case, the statement of October 16, 2014 (Exhibit rop 17-D7) was already available to the Opposition Division and reflects the essential aspects of Prof. K.'s argumentation, but the Opposition Division did not follow it. Thus, it is not a matter of the considerations put into the assessment of Prof. K. being presented for the first time, for instance, and the opposition division, which is

technically competent, not having been confronted with them yet. On the contrary, the essential arguments of the injunction plaintiff concerning the inventive step have already been presented to the opposition division, but have been judged by it to be unsustainable. The infringement court must accept this assessment as long as - as in this case - it cannot be established that the interpretations of the opposition division are objectively demonstrably incorrect, and it is also not evident that technically objectively incorrect conclusions have been drawn from an established fact.

(bb)

The same applies to the considerations as to whether the expert - also for ethical reasons - would have refrained from using a lower dose than the proven effective dose of 720 mg/day in further dose-finding studies because of the threat of irreparable damage in MS with progressive brain lesions. In this respect, too, it is not appropriate for the Senate to substitute its own - lay - considerations for those of the expert opposition division, which considered an optimization of the dosage regimen from the expert's point of view to be advisable. From the passages in the ICH Guidelines cited by the injunction plaintiff, it is also not possible to infer such in a clarity on the basis of which the Senate itself could determine that the opposition division would have assumed an incorrect basis. In the quoted passages of the Guidelines, the German translation states:

"The choice of study design and study population for dose-response studies depends on the stage of development, the therapeutic indication being studied, and the severity of the disease in the patient population of interest. For example, the lack of appropriate salvage therapy for life-threatening or severe diseases with irreversible consequences may preclude the conduct of studies with doses below the maximum tolerated dose on ethical grounds." (p. 5, penultimate paragraph)

"Parallel dose-response studies with placebo or placebo-controlled titration studies (very effective studies typically used for angina, depression, hypertension, etc.) would be unacceptable in the study of some diseases, such as life-threatening infections or potentially curable tumors, at least when effective treatments are known. [...] On the other hand, the use of low, possibly ineffective doses, or titration to the desired effect, may be unacceptable, since initial failure in these cases may mean a chance of cure lost forever." (p. 4, para. 2, second paragraph)"

The Senate is unable to conclude that the case of lack of appropriate rescue therapy referred to in the first quoted paragraph exists, nor that MS falls within the diseases referred to in the second paragraph, such as life-threatening infections or potentially curable tumors, where initial failure may mean a forever lost chance of cure.

Insofar as the injunction plaintiff claims that a further dose-finding study would have deliberately accepted the possibility that test subjects would be provided with an insufficient dose of active ingredient and would therefore remain therapeutically untreated, possibly with the consequence that they would suffer irreversible impairments, the overriding benefit of such a study is to be weighed up which, in the event of successful proof of the efficacy of a lower dose, would have freed countless patients from taking a significantly too high dose of

active substance over a long and unforeseeable period of time, with the risk of major side effects, which had not yet been eliminated at that time, and at least the unnecessarily high burden in metabolizing the active substance from a therapeutic point of view.

(cc)

Furthermore, the Senate cannot recognize that the Opposition Division, with its assumption that the results of the detailed phase II clinical study in humans presented by K. showed that an "activity plateau" had already been reached with the dosage of 720 mg/day, proceeded from an objectively incorrect basis which, moreover, made its statements appear unreasonable. The parties agree that a plateau in the sense that an improvement in efficacy can no longer be expected with an increase in dosage above 720 mg/day cannot be inferred from K.'s slides. Whether this is a contradiction to the statements of the opposition division can, however, be left open. The opposition division relies on this statement only for the argumentation that it is not a matter of a "try and see" approach (when conducting further routine trials) because the results of a detailed phase II clinical trial in humans are already available. This statement is true, as will be explained in more detail below, irrespective of any efficacy plateau recognizable to the person skilled in the art. Moreover, the assessment of the inventive step is in any case only concerned with finding a lower dosage than 720 mg/day, so that ultimately the question of whether the skilled person would also have considered a higher dosage is irrelevant.

(4)

Finally, it cannot be established that in the opposition proceedings against the patent-in-suit (e.g. new) promising aspects are opposed which could not yet be taken into account by the opposition division in the proceedings concerning the parent patent. In particular, it is true that the declaration of Prof. K. submitted by the injunction plaintiff according to Exhibit rop 17-D11 (citation D 73 in the opposition appeal proceedings) was not yet available in the proceedings before the Opposition Division and was in any case not assessed by the Board of Appeal, which only dealt with the revocation ground of inadmissible extension, in its decision. That this statement, however, deprives the decision of the opposition division on the parent patent of its basis and dictates a different decision in the opposition proceedings against the patent of invalidity in such a clear manner that the Senate could determine it itself with the means available to it cannot be ascertained. This also applies to the considerations of Prof. K., highlighted by the injunction plaintiff at the hearing, that the assumption of an activity plateau at 720 mg/day is not correct. In this respect, reference is made to the comments under (3) (b) (cc).

(5)

Ultimately, however, it can even be assumed that Prof. K. is to be followed in the fact that the study conducted by him showed a significant efficacy of DMF in the treatment of MS only for the daily dose of 720 mg, while the lower doses of 120 mg/day and 360 mg/day proved to be therapeutically ineffective. Furthermore, it can be assumed that the study did not reveal any correlation between the active substance dose and the occurrence of side effects for the expert and that therefore - precisely because of the availability of a DMF dose of 720 mg/day that is well effective and at the same time has comparatively low, tolerable side effects - there

was no reason, if only for purely economic reasons, to undertake costly phase III studies with a lower DMF dose. It is also irrelevant whether the assumption that the risk of side effects would not be significantly reduced with a lower dose of active ingredient can be substantiated at all. Prof. K. himself points out that the treatment groups in the study were relatively small and that nominal differences between the groups should therefore be interpreted with caution. In the opinion of the Senate, it may be assumed on the basis of this that the study results do not speak - positively - for a dose-dependent occurrence of side effects, but that such a connection, which the expert will consider in principle, was not thereby yet excluded with certainty.

According to the assessment of the Senate, there is generally an obvious connection for the skilled person between the amount of active ingredient and any side effects of its administration, which also suggests the consideration of favorably influencing the side effects by a lower dose of active ingredient in the case in dispute. Taking this route is not prohibited for the skilled person because it has been shown in WO 2006/037342 A2 in connection with the treatment of psoriasis that the side effects associated with the ingestion of DMF can be beneficially influenced by a specific pharmaceutical formulation. On the one hand, this is merely another option for the person skilled in the art to manage side effects, which will not dissuade him from doing what usually promises a favorable influence on side effects, namely lowering the dose of the active ingredient. Secondly, the injunction plaintiff itself attaches importance to the statement that the mechanisms of action of DMF in the treatment of psoriasis and MS are quite different. From this point of view it could appear quite doubtful from the expert's point of view whether the pharmacokinetic measures which have led to success in connection with the therapy of psoriasis also prove to be effective in the treatment of MS. That and why this should be the case is also not apparent from the injunction plaintiff's submission.

Even if the person skilled in the art actually had to assume that a lower amount of active ingredient would not reduce the risk of side effects, the fact remains in any case that although the study demonstrated the efficacy of a DMF daily dosage of 720 mg, there was no evidence that with this amount - by chance - the lowest significantly effective dosage of DMF had been met and found. After all, the study had skipped several possible dosage steps between the ineffective dosage (360 mg/day) and the proven effective dosage (720 mg/day), namely dosages of 480 mg/day and 600 mg/day, from which it could not be ruled out a priori that therapeutic efficacy would be found for them or for one of them. On the contrary, there was a certain expectation of success for the sole reason that it would have been a real stroke of luck if the first and lowest therapeutically effective dose had happened to be found with the daily dose of 720 mg tested - omitting several possible lower doses. From a technical-scientific point of view, there was therefore considerable reason to believe that the efficacy limit had not yet been determined with the study, but that this was awaiting further clarification. To pursue this in a further suitable study and to clarify the efficacy limit of DMF for its own sake may have been unreasonable from a purely economic point of view (because of the

associated costs). However, this does not make the project inventive. After the result of the study, the remaining gap in knowledge was clear and it was equally obvious what had to be done to close it.

Contrary to what the injunction plaintiff argues, it is not a matter of including a further dosage form in an extraordinarily extensive and lengthy phase III study, but rather of obtaining certainty, e.g. in a phase II b study, such as that on which the previously known study by K. is based, as to whether and which lower active ingredient dose is therapeutically effective. The benefit of such a lower active ingredient dose was, as Prof. K. himself admits in another context, that a patient would have to take fewer tablets a day and that he would also benefit from a lower dose with regard to the metabolism of the drug in the liver, potentially toxic degradation products and the effects on the kidneys and other organs (cf. Exhibit rop 17-D7, p. 4, para. 15). This point of view is of particular importance in the present case because patients affected by MS have to take medication over extraordinarily long periods of time, possibly even decades.

The injunction plaintiff can also not successfully counter that a clarification of the 106 lower efficacy limit is out of touch with life and should therefore not be taken as a basis for the assessment of inventive step. Even if all the benefits from a lower dose of active ingredient discussed above had to be disregarded, pharmaceutical research does not only take place for purely commercial interests by companies active on the market, but equally in scientific institutions whose motivation is not explained by possible yields of knowledge gained.

Against this background, the Senate has reservations about following the injunction plaintiff in her argumentation that the expert would at best have considered a dosage slightly below 720 mg/day as an alternative, with which an expectation of efficacy was associated from the outset. Precisely because the reduction of the active ingredient dose by a larger step would have significantly increased the benefits for a large number of patients suffering from MS, it may have been obvious for a skilled person to also include the dose of 480 mg, the efficacy of which was not yet known from the prior art, in his considerations. It may be true that the dosing steps did not have to take place at 120 mg intervals, but could in principle have been chosen differently. Since the previous studies had made use of the previous 120 mg steps, nothing inventive can be seen in taking up and retaining this dosage regimen. The same applies to the fact that the amount of active substance administered with each tablet would have been varied in the case of a changed total dose (instead of 3 x 120 mg: 2 x 240 mg). On the one hand, such an approach is not mandatory because the patient could also have been administered four tablets with an active ingredient quantity of 120 mg. On the other hand, Prof. K. did not see any obstacle in varying the amount of active ingredient administered with each tablet when he conducted his study, and the results of his study, in which he had already provided for single doses of 240 mg/day, also offer no indications for such concerns.

Insofar as the injunction plaintiff has countered the assumption that there was reason for the skilled person to clarify the efficacy limit of DMF for its own sake, this does not hold water in the case law of the European Patent Office, which rejects the so-called "try and see" approach. According to the case law of the European Patent Office, the consideration that the person skilled in the art would have adopted a "try and see" attitude at least can be a reason for not applying the concept of "reasonable expectation of success" and for denying inventive

step independently of it, because the person skilled in the art would prefer to check whether the possible solution he has devised works instead of abandoning the project because its success is not certain (see Rechtsprechungsbuch, 10th ed, I. D. 7.2 "try and see" situation with reference, inter alia, to T 333/97, T 377/95 of April 24, 2001, T 1045/98, T 1396/06, T 2168/11). In the present case, however, as discussed, based on the prior art, there is precisely no reasonable expectation of success on the part of the skilled person, so that - as was also assumed by the opposition division - the assumption of a "try and see" approach is not relevant. Apart from that, neither the cited presentation in the case law book nor the decisions cited by the patent attorney representing the injunction plaintiff in the oral proceedings (T-239/16, T847/07, T-2506/12) indicate that the "try and see" approach is generally no longer followed in the case law of the European Patent Office. Rather, it is always decisive whether the person skilled in the art would adopt a "try and see" attitude according to the circumstances of the individual case (cf. also Rechtsprechungsbuch, loc. cit., for the assessment of decision T-847/07).

III.

The decision on costs is based on Section 97 (1) of the Code of Civil Procedure (ZPO).

There was no need for a ruling on provisional enforceability because the present judgment, as a second-instance decision in proceedings for a preliminary injunction, is no longer subject to appeal (Section 542 (2) sentence 1 of the Code of Civil Procedure (ZPO)) and is finally enforceable without any special ruling.

A	B	C