The Rhineland Biopatent Gazette

brought to you by Michalski Huettermann & Partner Patent Attorneys - Issue 2/2018

Duesseldorf/Munich, **06 November 2018** The times they are a'changing – particularly in the Biopatent discipline. Biopatent professionals live in a quickly developing world, which is sometimes hard to keep pace with. Michalski • Huettermann & Partner Patent Attorneys have decided to produce relief to this situation, and are proud to present a new information service related to Patent issues in Biotechnology. This newsletter issues on an irregular basis in order to provide information with respect to actual events, as well as in-depth-analyses of long-term developments. Patent Attorneys from our firm explain the meaning of recent developments and decisions affecting the Biopatent community, and provide expert insight into what's going on behind the scenes. In this issue, Dr. Christoph Volpers reports on recent developments regarding the US generics and biosimilars legislative pathway, and Dr. Ulrich Storz discusses a recent decision by the Federal Patent Court, related to Sanofi's antibody Praluent, the outcome of which is markedly different than in the United States.

Waxman *against* Hatch in Hatch Waxman -

Former coauthors of generics US legislative pathway in confrontation mode

The legislative proposal by one of the architects of the Hatch-Waxman Act to effectively bar generic drug makers from challenging patents at the US Patent Trial and Appeal Board has not found consent of the bill's other named sponsor.

The Drug Price Competition and Patent Term Restoration Act, also known as "Hatch-Waxman Act" referring to its initiators and authors, Senators Orrin Hatch and Henry Waxman, was enacted in 1984 to establish a legal system for generic drug regulation in the US as amendment of the Federal Food, Drug and Cosmetic Act. The new Section 505(j) of the latter (codified as 21 U.S.C. 355(j)) outlines the process of filing an abbreviated new drug application (ANDA) for approval of a generic drug by the FDA, and was intended to provide some protection for drug innovators on one hand but also incentives for facilitated filing of ANDAs by generics manufacturers on the other hand.

In drug innovators' favor, the Hatch-Waxman Act introduced a new five-year data exclusivity period upon market approval of a new chemical entity, during which period the FDA cannot approve a generic version of the drug. In addition, the institute of patent term extension (PTE) was established to account for time

Federal Patent Court denies injunction for compulsory license

Praluent case decided differently than in the US

In Issue 6/2016 of this Gazette we reported about the compulsory license the Federal Patent Court of Germany (BPatG) ordered in the Isentress case. In a nutshell, Merck & Co demanded a compulsory license for the sale of its anti-HIV drug raltegravir (Isentress), which yet fell under the scope of Shionogi's European patent EP1422218B1,that protects dolutegravir (Ticay), to which Merck's drug is structurally similar.

At that time, the judges justified their decision with an urgent public interest to keep Isentress on the market, as it was authorized for some patient groups that were not covered by Shionogi's drugs. They further acknowledged that Merck had earlier offered 10 mn USD for a global license. already available.

The resulting compulsory license was the first one the court ordered in its 55-year history by way of a preliminary order. Quite understandably, the decision sent some shockwaves through the community.

Recently, French drugmaker Sanofi tried as well. Its anti-cholesterol drug Praluent (the anti PCSK9 antibody Alirocumab) falls under the scope of European Patent EP2215124B1 assigned to Amgen, which protects, *inter alia*, Amgen's competing antibody Evolocumab (Repatha).

The patent has the following independent claim:

> 1. A monoclonal antibody (..) that (...) competes for binding to PCSK9 with
> (a) an antibody comprising a HCVR SEQ ID NO: 49; and a LCVR SEQ ID NO: 23; or
> (b) an antibody comprising a HCVR SEQ ID NO: 67; and a LCVR SEQ ID NO: 12

+ from our firm +

MH partner will give lecture at Basel University

On Tuesday, Nov 27, 2018, MH partner Dr. Ulrich Storz will give a lecture at the University of Basel, titled "CRISPR Cas9 – Patentrecht und Ethik im Spannungsfeld." The lecture is part of a series of lectures by different speakers, titled „transformative technologies", organized by Professor Bijan Fateh-Moghadam.

The lecture will begin at 6.15 PM in Auditorium 101, Rheinsprung 9, 4051 Basel.

EQE seminar 2018

As in previous years, we will offer two two-day free preparatory courses for the C and D part of the European qualifying examination.

The courses take place on Monday / Tuesday, 26./27. November, and Saturday / Sunday, 8./9. December 2018

The courses content focuses on appropriate techniques and error prevention strategies to

the patented product is in clinical phase testing and under review by the FDA.

The generics industry gained the ability to obtain approval through ANDAs based on manufacturing information and bioequivalence studies, the ability to challenge brand drug patents prior to marketing in court while enjoying safe harbor from infringement lawsuits during ANDA preparation, and gained 180-day generic drug exclusivity for the first runner in the field receiving ANDA approval.

As key concepts of the Hatch-Waxman Act which significantly promoted introduction of generic drugs – from only 13% of total prescriptions in 1983 to 84% in 2012 – the innovator has to have relevant patents listed in the Orange Book and the generics company has to certify with respect to each patent in the list; upon "paragraph IV certification" claiming that a patent is invalid or not infringed by the ANDA product, the innovator is prompted to commence patent litigation against the generics entity who in turn can file countersuit to have respective Orange Book patents declared invalid.

In order to strike similar balance between innovation and affordability for *biologic* drugs, in 2009 the Biologics Price Competition and Innovation Act (BPCIA) provided incentives for biologic innovators and created abbreviated pathway for biosimilar makers.

In addition to said court litigation however, Inter-Partes Reviews at the Patent Trial and Appeal Board (PTAB) of the USPTO, created by the America-Invents-Act in 2012, have become an increasingly important institute over the last years to challenge and invalidate drug innovator patents independently of the litigation pathway tied to the regulatory approval process.

Last June, Senator Hatch proposed an amendment[1] entitled the "Hatch-Waxman Integrity Act of 2018" with the purpose to "ensure that Hatch-Waxman continues to operate as originally intended by protecting the ability of generic drug companies to develop low-cost drugs while at the same time ensuring brand-name companies have sufficient protection in place to recoup their investments". Allegedly, generic and biosimilar manufacturers were increasingly

Note that this claim is a so-called "competes with" claim, in which the claimed antibody is simply specified by its potency to compete for binding to a target with a reference antibody.

This claim type is a subtype of the "epitope based claim", type in which the antibody that is protected is not specified by structure, but merely indirectly, by the epitope it binds to on the respective target protein.

These types of claims are subject to an ongoing controversy, as their scope encompasses a vast amount of antibodies, including antibodies that the patent owner has never made himself.

Sanofi and Amgen are involved in a legal dispute in the United States related to corresponding US patents US8829165, US8859741, and others, all of which have as well epitope based claims (yet not of the even more controversial "competes with" type), and therefore encompass also Sanofi's drug:

> 1. An isolated monoclonal antibody, wherein, when bound to PCSK9 (...) binds to at least one of the following residues: S153, I154, P155, R194, D238, A239, I369,S372, D374, C375, T377, C378, F379, V380, or S381 of SEQ ID NO:3, and (..) blocks binding of PCSK9 to LDLR.

> 1. An isolated monoclonal antibody that (...) binds an epitope on PCSK9 comprising at least one of residues 237 or 238 of SEQ ID NO: 3, and (...) blocks binding of PCSK9 to LDLR.

While in the first instance, the District Court declared the patent valid and issued an injunction against Sanofi, estopping them from marketing Praluent, the Court of Appeals of the Federal Circuit (CAFC) first overturned the injunction on grounds of public interest, and then remanded the case back to the District Court, to re-examine the validity of the patent. In its decision, the CAFC ordered the District Court to reconsider if the genus claim (= the epitope claim) is supported by representative species (= sufficient examples of structurally defined antibodies that bind the epitope). It remains however unclear what a sufficiently large number of species is.

While the District Court's decision is still pending, the USPTO has already instructed its examiners no longer consider a newly characterized epitope as adequate written description for an antibody claim.

Meanwhile, Amgen has filed a petition for certiorari to the Supreme Court, alleging that the CAFC's ruling would result in "jurisprudential anarchy". Amgen claims that the patent act would require that a patent specification simply teaches others to make and use the invention, instead of demanding possession of invention. In fact, with this submission, Amgen is challenging that Written Description is a distinct requirement separate from the Enablement Requirement (as established in Ariad vs Lilly).

Epitope based claims in general, and this case in particular, are/is probably one of the most discussed topics among Biotech IP professionals these days. We have discussed these claims in panel discussions at the BioConvention, May 2018 in Boston, as well as at the C5 Life Science Summit in Munich in

successfully to successfully pass the C and D parts of the EQE exam.

According to our experience, well-prepared examination documents significantly increase the chances of success.

Therefore, we want to furnish the participants with the necessary knowledge.

In this respect, the course should be understood as an addition to a content-related preparation of the legal foundations of the EPC.

The courses take place in Dusseldorf in our premises in the Speditionstr. 21 and are free of charge. Speakers of the course are Dr. Torsten Exner, Dipl.-Ing. Andreas Gröschel and Dr. Aloys Hüttermann.

Registration is possible immediately. Please mention your full name, employer and the desired date, and send your application to ege@mhpatent.de.

Feedback please !

What do you think about this newsletter? Let us have your comments here.

Archive

To obtain a neat overview of the quickly changing world of Biopatents, find prior issues of the Rhineland Biopatent Gazette here.

utilizing IPR proceedings for patent invalidation while circumventing the HWA and BPCIA regimes, leading to added litigation pressure on innovator companies and giving generic companies who lost in Hatch Waxman litigation a second chance to challenge a drug patent ("getting a second bite at the apple").

Hatch's proposal aims to "close the loophole unintentionally created" by the AIA and "restore the careful balance" of the HWA and the BPCIA. According to the proposal, generics/biosimilar makers wishing to challenge a brand drug or biologics patent, and related entities ("any party in privity with the applicant"), will be required to (i) choose between the specific HWA/BPCIA patent procedures and the Inter Partes or Post-Grant Review proceedings under the AIA, rather than taking advantage of both; and (ii) not rely "in whole or in part on any decision issued by" the PTAB as evidence that the brand patent is invalid in the HWA or BPCIA procedures.

Said amendments to be made to Section 505 of the Federal Food, Drug and Cosmetic Act for chemical compounds and to Section 351(k) of the Public Health Service Act for biosimilar compounds would intend "to prevent the Inter Partes Review process for challenging patents from diminishing competition in the pharmaceutical industry and with respect to drug innovation".

The proposal is being heavily discussed and – of course – highly controversial. Enactment of the amendment would require an ANDA or biosimilar applicant to choose between engaging in the ANDA/biosimilar approval pathway or challenging a patent in an IPR or PGR proceeding. The latter have been perceived as faster and cheaper alternatives to long and costly countersuits. However choosing that route apparently would mean that the applicant would not any more be able to rely on the brand company's safety and efficacy studies for FDA approval, with drastic consequences for budget and time-lines. In Hatch's own words:
"*The party can file a Hatch-Waxman suit, which carries the benefits of being able to rely on the brand company's safety and efficacy studies for FDA approval, or file an IPR proceeding, which is cheaper and faster, and easier to win. But it can't do both*". [1]

October. Please request the slides here. See also Issues 4/2016 and 2/2017 of this Gazette.

Back to the German case. Sanofi had filed an action at the Federal Patent Court under § 24 and § 81 of the German Patent Act, to order a compulsory license under reasonable royalties. Further, Sanofi demanded a preliminary order under § 85.

§ 24 sets forth that a compulsory licensee may be awarded to a petitioner if the latter has unsuccessfully tried to obtain, within a reasonable period of time, a license from a patent proprietor, while the public interest demands such license.

§ 85 provides that compulsory licenses can be awarded by means of a preliminary order, provided that such license serves public interest.

The Court denied Sanofi's request. First, the Court found that Sanofi had not made sufficient efforts to obtain a license on reasonable commercial terms. Sanofi had made a short offer to Amgen on June 20, 2018, however, only three weeks later, on July 12, 2018, they filed the request for a preliminary order with the Court.

The Court also found that Sanofi should have started their attempts to obtain a license earlier, in particular because the corresponding infringement proceedings were resumed in December 2017 already, and because the study Sanofi referred to in order to demonstrate the public's interest in a compulsory license (which study showed that Praluent would reduce total mortality in high risk patients by 29%, compared to a Placebo) was available in March 2018 already.

Hence, the Court concluded that Sanofi's letter of 20 June 2018 would constitute a "last-minute offer", and would not fulfill the condition of "within a reasonable period of time", as set forth in § 24.

Second, the Court found that Sanofi did not sufficiently demonstrate that there was a public interest in the further free availability of Praluent, as they had failed to make convincing arguments that other products on the market - in this case, Amgen's Repatha, did not possess the (particular) therapeutic properties of Praluent in equal measure.

Note that this decision only referred to Sanofi's request for a preliminary order to award a compulsory license. However, the final determination of the merits of the case (3 Li 1/18) is still pending.

Notably, European Patent EP2215124B1 is opposed by 5 parties, among them Sanofi, Eli Lilly and Regeneron. Oral proceedings will take place at the end of November 2018.

The outcome of this case will be quite interesting, because here claims of the highly controversial "competes with" type will be at stake. The last major opposition case in which this claim type was at issue was the Opposition against BMS's patent EP2161336B1 (see this Gazette, issue 3/2017).

Last week now, Senator Henry Waxman announced that he will be "vigorously opposing" the idea of Hatch's amendment. Drug regulatory experts and IP specialists alike are keen to see how this concept will play out in view of these opposing stand-points and the fact that Senator Hatch is expected to retire in January 2019.

[1] "Hatch Amendment to Incentive Generic Drug Development", Senator Hatch Press Release, (June 14, 2018)

However, in that case, BMS cancelled the respective claim 3 in the course of the proceedings, so the Opposition Division did not have to decide upon it.

It will also be interesting to see whether the recent developments in the United States, raising the bar to such type of claims, have an influence on the Opposition Division's decision.

The Division's preliminary opinion, however, which issued December 13, 2017, suggests that the patent will likely be maintained in unamended form.

MH Patent is getting personal... Today: Wasilis Koukounis

Wasilis Koukounis graduated in Mechanical Engineering and in Sales Engineering and Product Management from the Ruhr-University Bochum. At the Heinrich Heine University of Düsseldorf, he also completed the Master's degree in Intellectual Property.

He gained technical professional experience at an international precision casting group and at a shipyard, both in the research and development department. Since 2011, he has been active in intellectual property law and began his training as a patent attorney in a patent and law firm. After having qualified as a patent attorney, he worked as a freelance patent attorney and as a counsel patent attorney for a DAX conglomerate. There, he was responsible for the business units Mining, After-Sales-Management and Wind Turbines. He also conceptualized a new IP strategy for the conglomerate across all business units. In 2018, he joined the patent law firm Michalski Hüttermann & Partner.

His main areas of practice include prosecution and litigation matters of technical protective rights. Further focuses of his work are the employee invention law, trademark law and design law. He is also specialized in the areas of legal opinions, license agreement matters, conciliation negotiations, FTO analyses, IP strategy consulting and patent portfolio management.

Wasilis Koukounis was born in 1985 in Bochum and lives in Düsseldorf. He speaks German, English and Greek. In his spare time, he is committed to charitable work and likes to cycle.

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