The Rhineland Biopatent Gazette

brought to you by Michalski Huettermann & Partner Patent Attorneys - Issue 1/2019

Duesseldorf/Munich, **22 February 2019** 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, we discuss a new chapter in the epic patent litigation history related to adalimumab patents, the revocation of Broad Institute's 2nd CRISPR Patent, and amendments suggested by the European Commission to the SPC directive.

New battlefronts in the adalimumab patent epic

how a biosimilar company becomes the prey of another biosimilar company

More than one time we have discussed new developments in the adalimumab patent battles.

In issue 8/2017 of this Gazette, we reported that Amgen, who is the maker of the adalimumab biosimilar AMGEVITA®/ AMJEVITA®, settled with AbbVie, the maker of world's blockbuster No 1, the anti TNFα antibody HUMIRA®, and holder of a large patent portfolio protecting the drug, its indications, dosages and formulations.

See our article in Human Antibodies 25, which discusses AbbVie's patent strategy to protect Humira from biosimilar competition. Please ask for a copy here.

Now, this does not mean that Amgen is out of the crosshairs of adalimumab IP stakeholders.

On January 28, 2019, US company Coherus BioSciences announced that it has become the latest adalimumab biosimilar developer to settle with AbbVie. Under the agreed terms, Coherus' product, which is not yet approved, will be able to launch in the United States on December 15, 2023.

But that's not all. Coherus further announced that it has sued Amgen for infringement of its adalimumab formulation patents US 10,155,039, 10,159,732, and 10,159,733. Although Amgen's Amjevita is not yet available in the United States, it is

EPO Opposition Division revokes Broad's 2nd CRISPR Patent

failed priority claim keeps being a problem

Last week, on February 14, 2019, the 2nd patent out of Broad Institute's CRISPR Cas9 patent family was revoked. The Patent, EP2784162B1 had the following independent claim:

> 1. An engineered, non-naturally occurring Clustered Regularly Interspersed Short Palindromic Repeats (CRISPR)-CRISPR associated (Cas) (CRISPR-Cas) vector system comprising one or more vectors comprising:
> a) a first regulatory element operably linked to one or more nucleotide sequences encoding one or more CRISPR-Cas system polynucleotide sequences comprising a guide sequence, a tracr RNA, and a tracr mate sequence, wherein the guide sequence hybridizes with one or more target sequences in polynucleotide loci in a eukaryotic cell,
> b) a second regulatory element operably linked to a nucleotide sequence encoding a Type II Cas9 protein,
> wherein components (a) and (b) are located on same or different vectors of the system, wherein the CRISPR-Cas system comprises two or more nuclear localization signals (NLSs) expressed with the nucleotide sequence encoding the Cas9 protein, whereby the one or more guide sequences target the one or more polynucleotide loci in a eukaryotic cell and the Cas9 protein cleaves the one or more polynucleotide loci, whereby the sequence of the one or more polynucleotide loci is modified.

The patent was opposed by 8 opponents. In the summons to oral proceedings, the Opposition Division had already declared that it would adopt the preliminary position that the priority claim is invalid, for the same reasons as in Broad's earlier patent from the same family, EP2771468B1 (we have reported on this case, too).

In a nutshell, inventor Marraffini, who was a co-applicant of *inter alia* the oldest priority application, had not transferred his priority rights to the applicants of the PCT, Broad Institute, MIT and Harvard University, but to Rockefeller University.

Due to the resulting loss of the priority claim, novelty-destroying prior art published in between became applicable. The Opposition Division

+ from our firm +

Save the Date: The 11th Rhineland Biopatent Forum will take place on June 6, 2019

Again, the seminar will take place in our premises in Düsseldorf.

Confirmed speakers are Andri Hess of Homburger Lawyers, Zurich, who will speak on the experiences with the newly created Swiss Patent Court.

Further, Matthew Heberling of Peptone will speak about the added value Artificial Intelligence can provide for antibody patent purposes.

And Dr Christoph Volpers, member of the firm and chair of our Frankfurt office, will speak about new developments in the European SPC legislation.

We are currently finalizing the speaker panel, and will keep you tuned. Send us an email here if you want to confirm your attendance already now.

already on the market in Europe, and Coherus claims that the production in the US would infringe their respective patents. Coherus has demanded damages and an injunction.

In fact. Amgen's formulation differs from the formulation of Humira, as it has the following recipe:

- 40 mg/0.8 ml adalimumab
- 36 mg sucrose
- 0.4 mg polysorbate 80
- 0.24 mg glacial acetic acid
- NaOH for pH adjustment to 5.2

Coherus' patents have the following independent claims:

> 1. A stable aqueous pharmaceutical composition comprising:
> a) adalimumab;
> b) a buffer;
> c) polysorbate 80; and
> d) a sugar,
> wherein the composition is free of i) mannitol, ii) citrate and phosphate buffers, and iii) sodium chloride and wherein the composition has a pH of about 5 to about 6. (US10155039)
>
> 1. A stable aqueous pharmaceutical composition comprising:
> i) adalimumab;
> ii) a buffer; and
> iii) a stabilizer;
> wherein the composition is free of mannitol and has a pH of about 5 to about 6. (US10159732)
>
> 1. A stable aqueous pharmaceutical composition comprising:
> i) adalimumab;
> ii) a single buffer;
> iii) a surfactant; and
> iv) a sugar,
> wherein the composition is free of mannitol and has a pH of about 5 to about 6. (US10159733)

It seems that the common feature of these claims is that they are "free of" mannitol or the citrate/phosphate buffer as provided in the HUMIRA formulation.

Not very innovative, one might think, considering the relatively late priority date of this family (7 Sept 2012).

See again our article in Human Antibodies 25, for different patents claiming alternative adalimumab formulations.

Generally, this case shows the shift that is currently taking place in the biologics filed. Once a biologic is off-patent, the IP disputes are shifting from originator vs biosimilar to biosimilar vs biosimilar.

This development has so far not been seen in the small molecule business, where the battlefronts are still between originators and generics.

And why is this so? Maybe, because there is probably more science in making a biosimilar than there is in making a small molecular generic.

maintained its position regarding the loss of the priority claim, despite several experts who opined that the validity of the priority claim should be subject to the legal provisions of the country of origin (i.e., the USA).

We have discussed the underling legal problem in two articles (J Biotechnol. 2018 Jan 10;265:86-92, and Lles Nouvelles, Volume LIII No. 2, June 2018). Please send us an email if you would like to have copies thereof.

The oral proceedings against Broad's second patent lasted two days, after which the patent was revoked in its entirety, despite >35 auxiliary requests the patent proprietor had submitted.

The very same day, Broad filed an appeal against this decision.

As already discussed, the failure of the priority claim will likely affect Broad's other EP family members, although Broad may be able to restore novelty over the intermediate art by relying on claim features which are disclosed in the underlying PCT and confer novelty over the intermediate art.

And, as discussed in this Gazette, Issue 5/2017, the corresponding PCT application Rockefeller University has filed with Broad Institute, MIT and Harvard University as co-applicants could be the key to regain lost territory, because this family does not have the priority problem discussed above.

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European Commission plans major revision of the SPC Regulation

After patent expiry, production of SPC protected drugs for export could become legal

The European Commission has recently announced plans to effect an amendment to the SPC regulation, by introducing a Supplemental Protection Certificate (SPC) manufacturing waiver.[1] The suggested changes are intended to improve the business opportunities for EU-based generic and biosimilar companies in view of an alleged competitive disadvantage vis-à-vis their overseas counterparts.

The proposal would allow EU-based companies to produce and store generic or biosimilar products during the SPC term of a branded drug, provided this is done for the purpose of exporting that generic or biosimilar to a non-EU market where protection has expired or never existed.

There is hence quite some conflict potential in the proposal, although we have seen in the past years that the borders between originators and generic/biosimilar companies have blurred, with more and more originators acquiring a generic/biosimilar shop (Novartis/Sandoz, Pfizer/Hospira) or developing a biosimilar business themselves (Amgen). We will discuss this topic at the 11th Rhineland Biopatent Forum, which has been scheduled for June 6, 2019. See our "save the date" information in the "from our firm"-section of this Issue.

[1]Proposal for a regulation of the European Parliament and of the Council amending Regulation (EC) No 469/2009

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.

MH Patent is getting personal... Today: Dr. Jan Winkelnkemper

Jan Winkelnkemper studied biology and neuroscience at University of Bonn and completed his studies with his master thesis in the field of electrophysiology. He received his doctorate in Bonn in 2018 at the Institute of Zoology with a thesis on signal perception and processing of brainstem neurons.

During his Ph.D. he found his personal interests and strength back in IP and started to enthuse with the profession as patent attorney. In early 2019, he decided to start his training in intellectual property law at the law firm of Michalski Hüttermann & Partner.

Jan Winkelnkemper grew up in Bad Münstereifel and speaks German and English as well as reasonable French. Out of the office, he likes doing sports with a special passion for basketball. He likes nature and enjoys mountain biking together with his wife, dog and horse.

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