The Rhineland Biopatent Gazette

brought to you by Michalski Huettermann & Partner Patent Attorneys - Issue 2/2016

Duesseldorf/Munich, **23 March 2016** 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, MH Partner Dr Torsten Exner discusses decision T 2220/14, while Dr. Christoph Volpers and Dr. Ulrich Storz put a spotlight on etanercept biosimilars.

Genetic Engineering Claim stands heavy fire

T 2220/14 sets the bar high for sufficiency/enablement attacks

It can be a real life-saver for patentees that there is no written description requirement at the European Patent Office (EPO). For the well beaten paths of genetic engineering the Boards of Appeal (BoA) meanwhile rate the skilled artisan's knowledge rather high.

In decision T 2220/14 ("VelocImmune mouse"), BoA 3.3.08, one of the Boards that has competence over life science cases, had to decide, *inter alia*, on enablement/sufficiency attacks on a method claim that involved genetic engineering of stem cells. The underlying patent EP1360287B1 is assigned to Regeneron, and challenged by Kymab, Merus and Novo Nordisk.

The claim recited a method of modifying an endogenous Ig variable region gene locus in an isolated mouse embryonic stem (ES) cell. The claimed method involved in situ replacing V, D, and J gene segments of the endogenous locus with orthologous human V, D and J gene segments. One claimed step was creating a "large targeting vector for use in a mouse ES cell (LTVEC)", which was then to be introduced into a mouse ES cell.

The opponents essentially argued that the patent did not put the skilled artisan into a position where he/she carry out the claimed method. He/she could not obtain – in a single stretch of genomic human DNA – all of the human V and J, or V, D and J

The last Mohican of antibody(-like) compound patents

Etanercept veteran patent subject of multilateral battle

Amgen's anti TNFα Fc fusion peptide etanercept (Enbrel®) is one of the six best-selling antibody-derived therapeutics in the world (the others being Rituximab, Infliximab, Adalimumab, Trastuzumab and Bevacizumab), with global sales of 1.34 bn USD in the last quarter of 2015 alone.

Etanercept will be the only one which will continue to run under compound patent protection beyond 2020 - until 2028, to be precise.

This is because on Nov 22, 2011, Amgen received the issuance of US Patent 8,063,182 B1 assigned to Roche but exclusively licensed to Immunex (which is a 100 % subsidiary Amgen acquired in 2002 for about 16 bn USD).

The issuance extended the time under which etanercept is protected until 2028 – while the underlying priority application was already filed September 12, 1989.

The grant sent a series of shockwaves into the Biopatent community, also to Sandoz, who at that time had already an etanercept biosimilar program in the pipeline, expecting a much earlier compound protection expiry in the US. The grant came utterly surprising because due to the early priority date, the underlying application 08/444,790 had not been published upfront.

On August 22, 2015, the Coalition for Affordable Drugs V LLC, a company run by Hedgefond Manager Kyle Bass, filed a petition for Inter Partes Review (IPR) challenging the validity of said patent (Coalition for Affordable Drugs V LLC v. Hoffman-LaRoche Inc., IPR2015-01792). Bass's strategy consists of filing IPRs against key patents of a given pharmaceutical target company while betting on a drop in that target's share price.

On March 11, 2016, the Patent Trial and Appeal Board (PTAB) denied institution of said IPR for failure to establish a reasonable likelihood that Bass would prevail in showing the unpatentability of any of the challenged claims.

Amgen might be particularly delighted about this rejection

+ from our firm +

Christoph Volpers to speak at Forum on Pharmaceutical Patent Term Extensions

Dr. Christoph Volpers will be a speaker at the C5's 15th International Forum on Pharmaceutical Patent Term Extensions in Munich on June 21/22, 2016.

He will be elaborating upon the "Two Sides of the same Coin – Deciphering the Extent of Protection for Biologics".

Find more details on the conference here.

9th Rhineland Biopatent Forum to take place June 2, 2016

The 9th Rhineland Biopatent Forum will take place June 2, 2016 in our office in Duesseldorf. Again, we were able to recruit a panel of high profile speakers.

Dr. Dorian Immler, Head of Patents Pharma, Consumer Health & Animal Health, Bayer Intellectual Property GmbH, will speak about the difficulties of enforcing 2nd medical use patents.

Filip de Corte, PhD,

gene segments of a human IgG locus, and insert this to precisely replace the endogenous variable region gene in one step at the priority date. It had not been known which specific V, D and J segment was orthologous to a given mouse V, D and J segment. Even the 5' location of the mouse Ig loci had not been conclusively known. A suitable vector had also not been available at the priority date. In contrast, the patent only had a single hypothetical Working Example which had been put into practice only much later, as evidenced by two subsequent scientific articles by the inventors. This hypothetical Example furthermore used serial LTVECs.

The Board firstly held that the pertinent disclosure was the entire technical information of the application as a whole, which went beyond Example 3. As for the two scientific articles: they could not establish that the approach suggested in Example 3 would not work. There was also nothing wrong with a "prophetic" example. There was no requirement in the EPC that the applicant must have carried out the claimed invention. The only relevant question was whether a person skilled the art, following the teachings in the application as filed, supplemented with his/her common general knowledge and with a reasonable amount of experimentation, including some trial and error, would be able to carry out the invention as claimed at the relevant date.

A general note good to hear from an Appeal Board: The assessment of sufficiency of disclosure (enablement) has to be conducted in each case on its own merits. The facts of the case need to be correlated to certain general parameters, e.g. the amount of reliable technical details disclosed in the application, the time when the disclosure was presented to the public and the corresponding common general knowledge, as well as the character of the technical field and the average amount of effort necessary to put into practice a certain written disclosure in that technical field. In a technical field as highly complex as at hand, the average amount of effort necessary to put a written disclosure into practice were in any case rather high and involved a considerable amount of trial and error.

It is also worth to have a look at the Board's definition of the skilled artisan in this case: we talk about a team of specialists with

because shortly before that decision, on February 26, 2016, they had filed suit against Sandoz at the District Court of New Jersey (Immunex et al v. Sandoz et al., 3:16-cv-01118) for patent infringement. In said suit, Amgen asserted, *inter alia*, infringement of the '182 patent (plus another "submarine" patent claiming the same priority, namely US 8,163,522, which will expire even later, namely 2029), and alleged that Sandoz failed to comply with the "patent dance" provisions of the BPCIA (see Issues 3/2015 and 6/2015 of the Rhineland Biopatent Gazette).

The BPCIA (Biologics Price Competition and Innovation Act) had been enacted in 2009 and established an approval pathway for biosimilars involving a procedure for patent dispute resolution between the originator (reference product sponsor) and the biosimilars manufacturer. The patent dispute resolution procedure, also casually termed "patent dance", involves a complicated, multi-step patent information exchange process, aiming at a mutually agreed list of patents to be immediately litigated, and triggered by disclosure of the application dossier and manufacturing information to the originator.

In contrast to its filgrastim (Neupogen®) biosimilar application before, where Sandoz refused to disclose its application to the reference product sponsor and to participate in the "patent dance" at all, in the case of its etanercept biosimilar candidate Sandoz engaged in the initial steps of the "patent dance" after the biosimilar company had made regulatory application documents available – albeit not to the degree the reference product sponsor had expected:

> "The manner in which this database access was provided would not have allowed Immunex local access and evaluation except after manual download of the thousands of documents included therein, along with a folder-by-folder manual reconstruction of the database's directory structure."

One needs to remember, however, that according to the CAFC ruling from July last year, disclosing the abbreviated Biologics License Application (aBLA) and manufacturing information and triggering the "patent dance" was concluded to be *not* mandatory for the biosimilar applicant.

It appears that Sandoz was served with Amgen's complaint on February 26, 2016, which, under 35 USC § 315(b), leaves them a year to file their own Inter Partes Review petition against the '522 patent.

In 2013, when the Phase III trials started, Sandoz had already sought a Declaratory Judgement against Amgen at the Northern District of California (Sandoz v. Amgen and Roche, 3:13-cv-02904), claiming that (i) the sale, offering of its etanercept product would not infringe any claim of either the '182 or the '522 patent, (ii) both patents were unenforceable and (iii) both patents were invalid.

The district court dismissed the demand because Sandoz failed to establish a "case or controversy" as required to obtain declaratory relief, because no infringement was imminent in the recently launched Phase III, and because neither party could institute patent litigation until the BPCIA patent exchange procedures were completed The CAFC confirmed that decision, which therefore does not provide any guidance with respect questions of infringement or validity.

It is hence interesting to see how an old war horse, as Amgen's patent, engages in battle in the autumn of its career.

And in Europe ? While Sandoz has announced in Decem-

Head Intellectual Property Crop Protection, Syngenta International AG, will speak about the phenomenon that patent attorneys sometimes forget that patent law operates in a context of other laws as well as a social, political and economic context

Our colleague, Konstantin Linnik, PhD, Partner at Nutter McClennen & Fish LLP, Boston, will speak about the recent patent disputes in one of the most commercially promising disciplines of Biotech, Immunooncology.

Partners and associates of our firm will also present on selected topics. Dr. Andreas Hübel will speak about IPR aspects of an "unclassyfiable" class of drugs, namely vaccines.

Dr. Christoph Volpers will discuss the "Patent Dance" approach practiced in the approval of Biosimilars in the US.

Dr. Ulrich Storz will address the question whether Biotech is ripe for patent pools. He will do this on the example of NIPT (non invasive prenatal testing) and the hyped CRISPR/Cas technology.

Participation is free of charge, but we will enroll applicants on a first serve basis. If you would like to attend, please send us an email here.

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.

knowledge and capabilities in the fields of genetic engineering, immunology and mouse embryology and genetics, and in particular ample experience in bacterial homologous recombination and targeted recombination in eukaryotic cells.

ber 2015 that the EMA has accepted an application for approval of their etanercept biosimilar, Biogen and Samsung Bioepis have already received EC approval for their respective biosimilar, called BENEPALI®, in January 2016. Reportedly, market launch has started in the UK in February 2016 already.

Michalski · Huettermann & Partner are getting personal... Today: Dr. Nicole Giesen

Nicole Giesen, born in 1970, studied chemistry at the RWTH Aachen. After working and studying in Aachen and Leeds, she finished her studies with her PhD thesis in 2001 in the field of metalorganic asymmetric chemistry. Additionally, she holds a bachelor' s degree in business administration.

Nicole Giesen is co-author of several publications in the field of metalorganic chemistry and X-ray analysis of metal complexes. Dr. Giesen is a chartered German patent attorney since May 2005. Since 2005, she has been admitted to practice as European Trademark Attorney at the European Trademark Office (OHIM). Since 2006 she is a European Patent Attorney and has been admitted to practice at the European Patent Office (EPO). She speaks German and English.

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