# The Rhineland Biopatent Gazette

brought to you by Michalski Huettermann & Partner Patent Attorneys - Issue 2/2017

**Duesseldorf/Munich**, **11 April 2017** 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 give an update on the CRISPR Cas dispute, and report about a development which might, unexpectedly, render the Unitary Patent Court more attractive.

## Charpentier's/Doudna's EP CRISPR patent granted

Is way cleared for patent pool ?

On April 7, 2017, the European Patent Office has mentioned the grant of European Patent EP2800811, despite earlier problems during prosecution (see Issue 7/2016 of this Gazette). The patent is assigned to, *inter alia*, the University of Berkeley, and with Emmanuelle Charpentier and Jennifer Doudna as two of the named inventors. Claim 1 of the patent reads as follows:

1. A method of modifying a target DNA, the method comprising contacting the target DBA with a complex comprising
a) a Cas9 polypeptide and
b) a single-molecule DNA targeting RNA comprising
(i) a DNA-targeting segment comprising a nucleotide sequence that is complementary to a sequence in the target DNA, and
(ii) a protein-binding segment that interacts with said Cs9 polypeptide,
wherein the protein-binding seqment comprises two complimentary stretches of nucleotides that hybridize to form **a double stranded RNA (dsRNA) duplex**
wherein the two complementary stretches of nucleotides are covalently inked by intervening nucleotides,
wherein said contacting is in vitro or in a cell ex vivo, and
wherein said modifying is cleavage of the target DNA

In contrast thereto, claim 1 of US patent No 8,697,359 assigned to Broad Institute (with Feng Zhang as main inventor), which was recently maintained in interference proceedings (see this Gazette, issue 1/2017) reads as follows:

1. A method of altering expression of at least one gene product comprising introducing into a **eukaryotic** cell containing and expressing a DNA molecule having a target sequence and encoding the gene product an engineered, non-naturally occurring Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)—CRISPR associated (Cas) (CRISPR-Cas) system comprising one or more vectors comprising:
a) a first regulatory element **operable in a eukaryotic cell** operably linked to at least one nucleotide sequence encoding a CRISPR-Cas system guide RNA that hybridizes with the target sequence, and
b) a second regulatory element **operable in a eukaryotic cell** 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, whereby the guide RNA targets the target sequence and the Cas9 protein

## Return of the Patent Death Squad

Recent invalidations of antibody patents by UK courts could motivate applicants to increasingly use the Unitary Patent System

After enactment of the Inter Partes Review (IPR) system in 2012 in the US, the first years saw revocation rates of > 60 %, which is significantly more than the steady 30 % revocation rate in EPO oppositions.

The Patent Trial and Appeal Board (PTAB) has for this reason been nicknamed "patent death squad", e.g., by former CAFC chief judge Randall Rader.

While recently, the PTABs revocation rates seem to reach somewhat more normal ranges, it looks as if the "death squad role" went over to UK courts, at least when it comes to patents protecting second generation embodiments of therapeutic antibody products, like dosage patents and formulation patents.

UK courts have in the recent years invalidated the national parts of quite a few such patents related to blockbuster antibodies, like Herceptin and Humira, and some of these decisions overturned prior decisions by the European Patent Office. See the following table:

| Patent No | Drug | Subject matter | UK court decision |
|---|---|---|---|
| EP1210115 | Herceptin | dosage | revoked in 2nd instance. [2015] EWCA Civ 57 (Hospira vs Genentech) |
| EP1308455 | | purity level | revoked in first instance [2014] EWHC 1094 (pat) (Hospira vs Genentech) |
| EP1516628 | | formulation | claims 1 to 6 revoked [2014] EWHC 3857 (pat) (Hospira vs Genentech) |
| EP2275119 | | | revoked in 1st instance [2014] EWHC 3857 (pat) (Hospira vs Genentech) |
| EP1944322 | Humira | dosage | although patents already withdrawn by assignee, judge found their subject matter invalid [2017] EWHC 395 (Pat) (AbbVie vs FKB and Samsung) |
| EP1406656 | | dosage | |

Now the Unitary Patent System is about to become reality hopefully still this year, mainly pending ratification by the UK (which has been somewhat compromised by the Brexit).

**+ from our firm +**

**10. Rhineland Biopatent Forum (June 8, 2016): Few places still available!**

The 10th Rhineland Biopatent Forum will take place June 8, 2016, in our premises in Duesseldorf.

Dr. Ranjit Ranbhor, Dy. General Manager IPR, Sun Pharmaceutical Industries Ltd, India, will speak about the changing role, and acceptance, of IP in India, in particular for the Indian Pharma Industry.

Atushi Shiomi, PhD, JP Patent Attorney, Tsukuni & Associates, will preset new options for 2nd medical use claims in Japan.

Tilman Breitenstein, Director DSM Innovation Center Intellectual Property, Delft, will discuss the use of Trade Secrets in Biotech.

Violeta Georgieva, LL.M., Legal and Regulatory Manager, EuropaBio Brussels will present the EC's notice on certain

cleaves the DNA molecule, whereby expression of the at least one gene product is altered; and, wherein the Cas9 protein and the guide RNA do not naturally occur together.

The different patent claims nicely demonstrate the different achievements both groups have made in the development of CRISPR Cas technologies.

While the Charpentier group has created a crRNA/tracrRNA chimera (the claim language calls it „a double stranded RNA (dsRNA) duplex"), to make CRISPR Cas more easy to handle, the Zhang group has enabled the technology to be used in eukaryotes, *inter alia* by the application of nuclear localization signals (NLS), as set forth in claim 3 of the respective patent.

If one assumes that the scopes of these two patents would stand representatively for other membees of the two patent families, part of the fog that surrounds this epic dispute would be clearing.

Zhang's patents would be dependent of Charpentier's and Doudna's patents – or, as Jennifer Doudna said in a teleconference held by UC Berkeley: „The Broad Institute's patent is for green tennis balls, but the patent we will have is for all tennis balls.

Such situation is not unfamiliar in the patent world. Companies wanting to exploit CRISPR Cas in eukaryotes would need patents from both parties.

A patent pool would be an adequate approach to facilitate access to this technology, as already suggested by authors in April 2016, when the outcome of the different disputes was not yet forseeable (Usdin & Fishburn, „Throw CRISPR into a pool", Biocentury Innovations, Apr 28, 2016).

Until recently, it was hard to imagine that such pool could be established, given the deep battle lines drawn between the two parties. It may yet be that the recent developments have increased the likelihood of such pool.

The Unitary Patent Court (UPC) will have exclusive jurisdiction not only in infringement matters, but also in revocation matters, and not only for patents validated as unitary patents, but also for the conventionally validated bundle patents, if not opted out (see below).

So far, European Patents could only be invalidated centrally in opposition proceedings, which had to be initiated within 9 months after grant. If this term is missed, invalidation has to be done country-by-country, which is cost- and labor intensive, and may result in different outcomes in the respective jurisdictions.

Further, because pharmaceutical products need their time to enter the market, the window for filing an opposition is oftentimes closed already when the market impact of a respective patent becomes aware to competitors.

The central invalidation at the UPC prolongs this time window to cover the entire lifetime of the patent. In the pharmaceutical sector, this is considered a serious threat for the industry's most important assets, and is often recited as one argument to remain with the conventionally validated bundle patents, and chose the opt out system.

The latter makes these patents inaccessible for UPC jurisdiction, and leaves them in the jurisdiction of the seemingly more predictable national courts.

However, in view of the recent decisions issued by UK courts, which revealed a quite negative attitude towards patents protecting second generation embodiments of therapeutic antibody products (like dosage patents and formulation patents) decision makers should consider whether they may want to re-adjust their preferences. A dosage patent or formulation patent that is validated as a unitary patent is inaccessible for UK courts.

Unitary patents could hence be in a safe harbor, which grants protection from the UK "patent death squad". It is likely that, in decision finding regarding invalidity issues of antibody second generation patents, the UPC will rather rely on EPO case law than on UK case law.

In other words: Even if we do not know how expertised the UPC will be, let alone how it will treat dosage patents or formulation patents, things can't get any worse than at UK courts, at least for formulation patents and dosage patents.

articles of the Biopatent Directive 98/44.

Dr. Bettina Wanner, Bayer Intellectual Property GmbH, will speak about the Unitary Patent and risks and advantages through the eyes of a Pharma inhouse counsel.

Further, there will be sufficient time to network with biopatent colleagues.

Particpation is free of charge. Invitations have already been circulated, but a few places are still available.

Please send an email to Mrs Felsner if you want to take part, or need a full programme.

**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.

## EURIPTA® EEIG is getting personal... Today: Jan Sommer – MH Patent

Jan Sommer studied civil engineering with an emphasis on structural engineering and building material technology at RWTH Aachen and graduated in 2008. He then spent four years working for a major German construction group. His work ranged from researching and developing types of foundations for offshore wind turbines to planning energy storage technology. Jan Sommer joined the law firm of Michalski Hüttermann & Partner in 2012, beginning his training to become a patent attorney there and completing it in 2016. He has since also been authorized to practice before the European Union Intellectual Property Office. His main area of practice is developing patent applications and oppositions in the fields of mechanical engineering, mechanics, structural engineering and automotive technology. He also represents clients in oppositions and appeal proceedings and in infringement and nullity cases. His practice also includes filing trademarks and designs. Jan Sommer is a member of the Association of Intellectual Property Experts (VPP) and International Federation of Intellectual Property Attorney (FICPI). Jan Sommer is based in the firm's subsidiary in Munich.

MICHALSKI · HÜTTERMANN & PARTNER

Imprint: Michalski · Hüttermann & Partner Patent Attorneys, c/o: Dr. Ulrich Storz - email: st@mhpatent.de

Hafenspitze - Speditionstrasse 21 - 40221 Düsseldorf - Tel.: +49 (0)211 159 249 0 - Fax: +49 (0)211 159 249 20
Perchtinger Straße 6 - 81379 München - Tel.: +49 (0)89 7007 4234 - Fax: +49 (0)89 7007 4262