The Rhineland Biopatent Gazette

brought to you by Michalski Huettermann & Partner Patent Attorneys - Issue 4/2015

Duesseldorf/Munich, **02 November 2015** 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 Ulrich Storz reports about an initiative to comment on a guideline suggestion by IPAustralia, plus on a recent decision by the Patent Trial an Appeal Board.

Initiative to comment on guideline suggestion after Australian Myriad decision

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On Oct 7, 2015, the High Court of Australia delivered its decision in case D'Arcy v Myriad Genetics. Essentially, the court overturned an earlier decision by the Federal Court of Australia, and came to a similar conclusion as the US Supreme Court in Ass'n for Molecular Pathology v. Myriad Genetics, Inc. (the notorious "Myriad" decisions, see Issue 4/2014 of the Rhineland Biopatent Gazette) and decided that the claimed subject matter would not be patentable

Claim 1 of the patent in question (AU 686004) is as follows:

> „An isolated nucleic acid coding for a mutant or polymorphic BRCA1 polypeptide, said nucleic acid containing in comparison to the BRCA1 polypeptide encoding sequence set forth in SEQ.ID No:1 one or more mutations or polymorphisms selected from the mutations set forth in Tables 12, 12A and 14 and the polymorphisms set forth in Tables 18 and 19.

The court ruled that said claim is not a claim to the fact that specific mutations and polymorphisms in the BRCA1 gene are indicative of a predisposition to breast cancer and ovarian cancer. Nor ist he claim an applications of that fact. Instead, claim 1 1 is a claims to a product: an isolated nucleic acid which has one or more specific mutations or polymorphisms in the BRCA1 gene. The methods of isolating the nucleic acid were not new and were not claimed. The methods of identifying the mutations and polymorphisms in the BRCA1 gene were not new and were not claimed. Claim 1 is to any isolated example of the BRCA1 gene which discloses the characteristic – one or more specific mutations and polymorphisms in the BRCA1 gene that are indicative of a predisposition to breast cancer and ovarian cancer. For those reasons, the court concluded that there is a lack of invention in

PTAB maintains ImmunoGen's Kadcyla patent

IPR filed by Phigenix dismissed

In an article we have recently published in mAbs, entitled "Antibody-drug conjugates: Intellectual property considerations", we have reported about Atlanta based Phigenix, who attacked Genentech and ImmunoGen for sale of their new blockbuster, ado-trastuzumab emtansine, Kadcyla ®, which is an antibody drug conjugate consisting of the maytansinoid DM1 and Genentech's anti-Her2 antibody trastuzumab. Please inquire here for a reprint of said article.

Not only did Phigenix, who son their website claim that they "will leverage licensed patented technology to establish a strong first-mover advantage in Personalized Medicine and forge a lasting leadership position in the rapidly evolving cancer diagnostic and therapeutics industry", sue Genentech on Jan 31, 2014 for patent infringement of their own US patent 8080534 in the Georgia Northern District Court (1:14-cv-00287, case still pending).

It remains enigmatic who is behind Phigenix. It appears that this company is headed by Carlton D. Donald, Ph.D., but the other people behind that company are undisclosed. At least it appears that Phigenix has sufficient fund to challenge Genentech and ImmunoGen on different levels, as shown in the following:

Phigenix also filed requests for Inter Partes Review (IPR) in 2014 against Genentech's US Patent 7575748 (IPR2014-00842) and ImmunoGen's US patent 8337856 (IPR2014-00676), which both protect Genentech's ADC Trastuzumab emtansine (Kadcyla®).

Genentech has acquired a license from ImmunoGen for using the SMCC linker and

+ from our firm +

Article on Immune Checkpoint Inhibitors accepted by mAbs

MH partner Dr. Ulrich Storz has authored an article on IP issues of Immune Checkpoint Inhibitors.

Immune checkpoint inhibitors („ICI") are drugs that interfere with tumor escape responses. Some members of this class are already approved, and treated as future blockbusters already now.

Many companies have developed patent activities in this field. The article focuses on the patent landscape related to ICI, to make it a little bit less confusing. Please inquire here for a reprint of said article, which is however not published yet.

MH Patent launches new seminar series

MH patent have launched a new seminar series, called "Bergische Patentakademie". The seminar is directed to small and medium sized enterpries from the "Bergisches Land"

claim 1.

Fortunately, the Court avoided to allude to the „product of nature doctrine“, which the US Supreme Court so frequently referred to. In contrast, the Court found that the claimed substance was the information embodied in the nucleotides of the molecule, which as such was an inherent part of the molecule and not created by human action.

Shortly after the decision came out, the Commissioner of the Australian Patent Office published her proposed examination practice, based on the finding that a claim to an isolated nucleic acid that merely represents information coding for a polypeptide is not patent eligible. On this basis, the Commissioners suggests that the following are not patent eligible:

- Naturally occurring (human) nucleic acid sequences encoding polypeptides or functional fragments thereof - either isolated or synthesised
- Naturally occurring (non-human) nucleic acid sequences encoding polypeptides or functional fragments thereof - either isolated or synthesised
- cDNA
- Naturally occurring human and non-human coding RNA - either isolated or synthesised

However, the Commissioner proposed the following remain patent eligible as they do not merely represent information coding for a polypeptide:

- Naturally occurring isolated regulatory DNA (e.g. promoters, enhancers, inhibitors, intergenic DNA)
- Isolated non-coding (e.g. "Junk") DNA
- Isolated non-coding RNA (e.g. miRNA)
- Naturally occurring isolated bacteria
- Naturally occurring isolated virus
- Isolated polypeptides
- Synthesised/modified polypeptides
- Isolated polyclonal antibodies
- Chemical molecules purified from natural sources (e.g. new chemical entities, antibiotics, small molecules)
- Isolated cells
- Isolated stem cells
- Probes
- Primers
- Isolated interfering/inhibitory nucleic acids (e.g. antisense, ribozymes)
- Monoclonal antibodies
- Fusion/chimeric nucleic acids
- Transgene comprising naturally occurring gene sequences
- Vectors/microorganisms/animals/plants comprising a transgene

The Commissioner's suggestion is thus a quite narrow interpretation to the High Court's Ruling, and, fortunately, would create significantly less legal uncertainty than what we are currently facing in the United States. The Commissioner has

the DM1 toxin conjugated to Trastuzumab.

A conjugate of said toxin-linker combination with an antibody was protected, among others, by ImmunoGen's patent US5208020.

On December 9, 2014, the Patent Trial and Appeal Board (PTAB) of the USPTO denied institution of IPR2014-00842 against US7575748, on the grounds that Phigenix did not establish a reasonable likelihood of prevailing with respect to any challenged claim.

Phigenix' attacks were based on alleged obviousness in view of the Herceptin®/Trastuzumab label 1998, plus a couple of prior art documents. According to the Board, which applied the "broadest reasonable construction in light of the specification of the patent", Phigenix failed to explain adequately how, nor provided sufficient evidence indicating that, the teaching in the Herceptin®/Trastuzumab label that certain patients failed to respond to Herceptin® would have motivated an ordinary artisan to treat such patients using a Herceptin® (huMab 4D5-8) conjugate.

In contrast thereto, IPR2014-00676 against US8337856 was instituted on October 29, 2014. The PTAB found that Phigenix has demonstrated that there is a reasonable likelihood that it would prevail on the ground that claims 1-8 of the patent would have been obvious over some of the prior art documents in view of the Herceptin®/Trastuzumab label. This however is not a final determination on the patentability of the challenged claims. IPR proceedings were thus instituted. The case is ongoing at the moment.

However, what the above article did not mention yet is that last week, on October 27, 2015, the PTAB decided to uphold ImmunoGen's US patent 8337856. The PTAB found that Phigenix had not shown by a preponderance of the evidence that claims 1-8 of said patent would have been obvious over the provided prior art.

Phigenix had asserted that the patent claims were obvious over a prior art reference, Chari et al (1992), which disclosed immunoconjugates comprising a mouse monoclonal antibody that was coupled to a maytansinoid toxin. Phigenix went on by stating that an ordinary person skilled in the art would have found it obvious to substitute the antibody disclosed in Chari et al (1992) with Herceptin.

ImmunoGen provided evidence that indicated that conjugates copmprising trastuzumab and a maytansinoid immunoconjugates would have been expected to demonstrate unacceptable levels of toxicity in normal human liver tissue in patients, and referred to reference, Pai-Scherf (1999), on this behalf.

The PTAB argued that "Petitioner does not persuade us that a preponderance of the evidence establishes

region, where, as the saying goes, "every village has a world market leader."

The seminar comprises 3 evening lectures, each with a speaker from MH patent plus an external speaker, e.g., from customs authorities and the like.

We will discuss patents, trademarks and designs, and the requirements for grant thereof, plus international strategies and ways to enforce them.

Attendees who participated in all three lectures will receive a certificate.

The lectures will take place in the Museum "Plagiarius" in Solingen, right in the heart of Germany's most renowned area for cutlery and steel industry.

The first lecture will already take place on Nov 6, 2015, 6.00 pm, and the two further lectures will follow in biweekly intervals. Participation is free of charge.

Please send an email to Mrs Felsner for further information.

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.

invited third parties to comment on her proposed practice by Friday 6 November 2015.

MH patent have drafted the following comments which we will submit to the commissioner by Nov 6, 2015:

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"Dear Commissioner,

The German Biotech Industry is extremely concerned about the legal uncertainty that has arisen in the aftermath of the US Supreme Court's decision "Ass'n for Molecular Pathology v. Myriad Genetics".

Said decision has created irritations amongst examiners of the USPTO, and despite guidelines that have repeatedly issued by the office, led to a *de-facto* stay of the prosecution of patent applications relating to different types of biotechnology inventions.

In particular, the Supreme Court refers to what it calls "the very point of patents", which exist to promote creation, while products of nature would not be created, and „manifestations of nature would be free to all men and reserved exclusively to none".

While there is a logic in this sentence, the court seems to have overlooked that new pharmaceutic products will only be developed if they can be protected by patents. The latter are indispensable to recover the tremendous investments that are being made during drug development. Thus, denying patent protection to a particular class of inventions, in an attempt to ensure that these inventions remain free for all men, may result in a situation where nobody can use them – because they have never been developed and approved for medical use.

On this background, the German Biotech Industry appreciates the reasonable and farseeing approach IPAustralia's Commissioner has recently proposed, and fully supports its enactment.

Further, the German Biotech Industry dares to hope that, once enacted, this policy may also have a beneficial effect on the situation in the United States, which is barely tolerable as it puts in question the existence of an entire technical discipline which like no other industry depends on patent rights to protect their R&D investments, in order to ensure that new drugs and other products can and will still be developed in the future."

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that a skilled artisan would have had a reasonable expectation of success in 2000 that a Herceptin-maytansinoid immunoconjugate would be useful in the treatment of breast tumors in humans, as petitioner asserts."

Thuis decision has some spice in it because Phigenix has also filed an opposition against ImmunoGen's EP counterpart of US patent 8337856, EP2283867, on February 19, 2015. In the opposition, Phigenix alleges that the patent claims would lack novelty over WO0069460, and lack inventive step over, amongst others, Chari et. al (1992), or the Herceptin®/Trastuzumab label, in combination with other documents disclosing maytansinoid toxins.

While Phigenix largely relies on prior art that has already been considered by the office, their main line of argumentation is that (i) the selection of Trastuzmab and a maytansinoid would not be a specific selection that would provide novelty over WO0069460.

Further, they argued that (ii) Chari et al (1992), would indeed be the closest prior art, as it relates to a functional anti- cancer ADC comprising a maytanisnoid and a murine anti-ErbB2 antibody, thus rebutting Genentech's arguments according to which it was surprising that Trastuzumab retained it's cytostatic activity in an ADC, and would not be degraded to a mere targeting device.

A first decision in this case cannot be expected prior to mid 2016, but it is to be expected that the PTAB decision might at least be considered by the opposition Division.

Interestingly, on February 2015, Genentech received the allowance for another EP application of the same family, EP2283866, with an almost identical claim scope. The opposition term of this patent will be open until November 25, 2015.

At least, one can say that ImmunoGen's patent survived IPR. Considering the latest events, where hedge funds challenged the validity of some blockbuster patents after they had placed bets on falling stock prices, and taken the different standards the PTAB sets compared to district courts ("preponderance of the evidence" vs. "statutory presumption"), due to which the PTAB has already been nicknamed "patent death squad", it may somewhat calm down emotions against IPR because we have a case here where a blockbuster patent survived it.

Michalski · Huettermann & Partner are getting personal... Today: Dirk Schulz

Dirk Schulz, born 1966, has studied Physics at the Universities of Freiburg and Göttingen. He prepared his diploma thesis at the Max-Planck-Institut für Strömungsforschung in Göttingen. Then he worked on his doctoral thesis at the Universities of Freiburg and Würzburg where he received a Ph.D. in 1996.

He started his IP work in 1996 in a patent and law firm in Munich. In 1999 he was admitted as a German Patent Attorney, in 2000 as a Professional Representative before the European Patent Office. Until 2007 he was a Partner of a patent firm in Essen.

In 2007 Dr. Dirk Schulz joined Michalski Hüttermann Patentanwälte in Düsseldorf with main areas in software, mechanical engineering, process engineering, measuring and controlling, optics and laser, both in patent prosecution and enforcement. He also works in the fields of trademarks and designs.
Dr. Dirk Schulz speaks German, English and French.

MICHALSKI · HÜTTERMANN & PARTNER

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