The Rhineland Biopatent Gazette

brought to you by Michalski Huettermann & Partner Patent Attorneys - Issue 4/2016

Duesseldorf/Munich, **27 May 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. Andreas Hübel, discusses a class- action style" opposition against a Syngenta patent, and Dr. Ulrich Storz, summarizes two recent cases from the antibody IP battlefield.

"class action style" opposition against Syngenta patent filed

To be smashed or not to be smashed – another tomato case on the horizon ?

Following the decisions G 2/12 (Tomatoes II) and G 2/13 (Broccoli II) wherein the Enlarged Board of Appeals of the EPO clarified that the exclusion of essentially biological processes for the production of plants pursuant to Article 53 (b) EPC does not affect allowability of a product-by-process claims wherein a plant or plant material is characterized by an essentially biological process for its production, the European Patent Office issued patents including such claims. One such patent is EP1515600B1 being directed to:

> 1. A non-transgenic domesticated L.esculentum plant growing fruits with a content of flavonols in the flesh of the fruit that is greater than 0.5 µg/mg dwt and a content of flavonols in the peel of said fruit of at least 5 µg/mg dwt due to up-regulated flavonol biosynthesis in the fruit flesh of said plant and restored CHI expression in the fruit peel of said plant, wherein said non-transgenic domesticated L. esculentum plant is obtainable by introgressing the CHI gene and the flavonol biosynthesis pathway genes CHS, FSH and FLS of Lycopersicon wild accessions LA1963, LA2884 and LA1926 into a domesticated L. esculentum plant.

The patent and the mentioning of grant were published on August 12, 2015 after slightly more than 12 years of prosecution (filing date of the application was December 24, 2003), and the term for filing an opposition against said patent expired on May 12, 2016. And you may guess – of course an opposition was filed against the grant of this patent.

Already during the term for filing an opposition, the initiative "no patents on seeds" called attention to the patent and collected signatures for support of an opposition against said patent to be filed by either one of (i) "Kein Patent auf Leben!", (ii) ProSpecieRara and/or (iii) VereinARCHE NOAH. Interestingly, the initiative not only stressed Article 53 b EPC and Article 53 a EPC as reasons for opposition, but also referred to Articles 52, 54, 56 and 83 and very briefly indicated why the patent is deemed not to meet these patentability criteria.

News from the antibody IP battlefield

Epitope-restricted antibody claims are back, and Genentech strikes back in Kadcyla dispute

Amgen has recently received a 1st instance in an infringement a case against Sanofi at the district of Delaware against Sanofi and Regeneron (1:14-cv-01317). The dispute circled around Sanofi's and Amgen's anti PCSK9 antibodies, which bind to the receptor for low-density lipoprotein (LDL) that are used in the treatment of hyperlipidemia.

The two antibodies, alirocumab (Praluent®, Sanofi) and evolocumab (Repatha®, Amgen) received FDA approval in 2015 for lowering cholesterol where statins and other drugs were insufficient.

The patents Amgen relied upon are US8829165, claim 1 of which is as follows

> 1. An isolated monoclonal antibody, wherein, when bound to PCSK9, the monoclonal antibody 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 wherein the monoclonal antibody blocks binding of PCSK9 to LDLR.

and US8859741, claim 1 of which is as follows:

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

Hence, both patents define the antibody they protect neither by the target alone, nor by the antibody sequences, but by the epitope of PCSK9 the antibody binds to. These claims thus belong to the category of so-called "functional claims"

The decision, although 1st instance, again emphazises the importance of epitope-defined antibody claims, which can still be used once antibodies against the target as such are already prior art, and which provide broader scope of protection then antibody claims protecting the mere antibody sequence.

+ from our firm +

MHP has contributed to *amicus curiae* brief in the Supreme Court appeal in case Sequenom vs. Ariosa

This case, in which fundamental issues of patent eligibility regarding Biotech-related inventions are for the first time reheared by the US Supreme Court after his decisions Molecular Pathology vs. Myriad and Mayo vs. Prometheus, has already seen quite a few *amicus curiae* briefs. One such brief was filed on behalf of UK's BioIndustry association (BIA), backed by EuropeBio, AusBiotech, Swiss Biotech association, HollandBio, BIOTECanada and Japan Bioindustry Association.

The *amicus curiae* brief does primarily focus on the BGH decision Receptor Tyrosin Kinase (BGH X ZR 141/13) of January 19, 2016, which our firm has translated to be attached to said brief.

In said decision, the BGH, stated, *inter alia*, that

> "contrary to the decision of the US Supreme Court (566 US (2012) **Mayo v Prometheus**), a technical teaching which teaches the use of a discovery to achieve a certain object, is patent eligible under European and German law, regardless of whether the teaching comprises an "inventive surplus"

Subsequently two oppositions were filed the last day of the term for filing an opposition, the first one by Dr. Christoph Then (note that Dr. Then is also contact person of the initiative "no patents on seeds") and Dr. Ruth Tippe, whereas the second opposition was filed on behalf of ARCHE NOAH, Society for Preserving and Developing the Diversity of Cultivated Plants. The latter opposition refers to the former opposition and also submitted a copy of the former letter of opposition.

At a glance with respect to the grounds for opposition, it is deemed that the patent violates Morality and Ordre Public (Article 53 a EPC) as its subject matter should be deemed as a result of biopiracy considering that the Patentee did not mention the original source of the original plants. As such the patentee is alleged to have violated the provisions of the Nagoya Protocol on Access and Benefit-sharing. The opponent admits that the plants were obtained via the University of California, but states that they stem from Peru and Chile. Peru signed the Nagoya Protocol on May 04, 2011, ratified it on July 08, 2014 and is a member since October 12, 2014 when the Nagoya Protocol entered into force. Neither the USA nor Chile signed the Nagoya Protocol yet. Unfortunately, the opponent did not provide any reason as to why the Nagoya Protocol should be applicable to a patent application that was filed more than a decade earlier than the date the Nagoya Protocol entered into force and why it should be applicable with respect to non-member states of the protocol.

Concerning the exclusion of essentially biological processes from patentability under Article 53 b EPC, the opponent solely repeat the arguments already provided in the proceedings leading to the decisions G 2/12 (Tomatoes II) and G 2/13 (Broccoli II), but fail to substantially address and contest the arguments provided by the Enlarged Board of Appeals of the EPO in their decision leading to the restriction of the exclusion to essentially biological processes as such, but not to plants or plant material obtainable by essentially biological processes provided that the plant is not restricted to a single variety.

The arguments for lack of novelty and lack of an inventive step were kept brief in the opposition and it remains to be seen whether they are well reasoned and sufficiently substantiated.

In addition, the opponents deem that the claimed subject matter is a discovery rather than the result of human intervention despite the reference to the method for obtaining the claimed plant, and they also regard Article 123 (2) EPC as violated due to a typographical error in the table within the description and some kind of lack of clarity among the subject matters of granted claims 1 and 2 in the absence of an explicit reference in claim 2 to one of the two elements claim 2 refers to. Nonetheless, from a logical point of view, claim 2 can only concern one of the two elements but not the other without becoming apparently contradictory.

In the last years, it appeared that epitope-restricted claims had come somewhat out of fashion. At the BIO Intellectual Property Counsels Committee meeting in Cary, N.C., in Nov 2015, a speaker of Morgan Lewis LLP advised that structural antibody claims would be the far better option over epitope defined claims.

While sequence claims may be more established, they at least provide a narrower scope of protection than the epitope claims Amgen has successfully used against Sanofi.

Sanofi and Regeneron stressed that this decision is the first step in this ongoing litigation and does not impact the distribution of alirocumab.

However, Amgen is also trying to obtain a permanent injunction against Sanofi, to block Sanofi from selling their antibody unless the two sides sign a royalty agreement.

Analysts estimate that with such agreement, Amgen could obtain about 750 mn USD per year, based on a 3.9 bn USD sales estimate for alirocumab by 2023.

This decision, which Sanofi said it will appeal against, could also strengthen Bristol Myers Squibb's position in their lawsuit against Merck & Co (see this Gazette, Issues 3/2015 and 1/2016) One patent BMS relies on claims a sequence-wise specified antibody against PD-1, plus further antibodies that cross compete therewith for binding to PD-1.

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In the patent dispute between Genentech and Atlanta-based Phigenix, which circles around Genentech's ADC ado-trastuzumab emtansine (Kadcyla®), Genentech is now going into the offensive.

Genentech had been attacked by Phigenix both in the US (alleged infringement of Phigenix' patent US8080534, plus two IPR requests against the respective patents protecting Kadcyla, US7575748 and US8337856) and Europe (opposition against EP2283867). While both IPRs have turned out unsuccessful (see this Gazette, Issue 3/2016), Phigenix' basis for claim in the infringement action remains erratic. Claim 1 of Phigenix' patent is as follows:

> 1. A method for treating a breast condition in a subject, comprising administering to a breast tissue of the subject, a composition that (1) inhibits PAX2 expression or PAX2 activity, (2) expresses DEFB1 or (3) inhibits PAX2 expression or PAX2 activity and expresses DEFB1.

It appears that Kadcyla does neither inhibit PAX2 expression or PAX2 activity, nor express DEFB1. In a submission made with the Court on May 10, 2016, Genentech referred to results from the discovery process and stated that Phigenix would have no basis for alleging infringement.

Genentech stated that Phigenix had acknowledged that they had not tested whether Kadcyla would have the effects

> that goes beyond the purposeful use of the discovered law of nature. This is because **all technical activities rely on a purposeful use of laws of nature**"

It is hard to imagine a better-phrased approach to this problem.

It appears that no German Biotech Industry Association has backed said brief, nor has an individual brief been filed by a German Biotech Industry Association. This is surprising in view of the importance of the case for the whole sector, and the fact the German BGH may have found the language which could change things to the better.

Report of Biopatent Expert Group mandated by the European Commission is now online.

On May 17, 2016 the Final Report of the Expert Group on the development and implications of patent law in the field of biotechnology and genetic engineering was published. The Expert Group was set up upon a decision of the EU Commission in November 2012 and now reports on plant related inventions, patentability of human stem cells, and the scope of protection of nucleic acid related inventions. Find the report here.

The USPTO has now released new Subject Matter Eligibility Examples

In the May 2016 update, the USPTO has provided further examples illustrating the subject matter eligibility analysis for various aspects of Life Science-related technologies. The updated examples provide hypothetical patent claims that either meet or do not meet subject matter eligibility in accordance with the Guidelines. Find the examples here.

Feedback please !

Moreover, Article 83 isallegedly contravened, because claim 1 recites ranges for the flavonol content in flesh and peel of the fruit which are ranges having an open upper end. Since the patent does not specify how a ridiculous content of flavonol in the fruit can be obtained, the claimed invention shall not be disclosed in such a way, that the skilled artisan can implement it.

We will keep you posted on these proceedings. For the time being it appears that the oppositions filed by the pressure groups improved, compared to oppositions in earlier case, but for what reason ever do not meet the standards applied by professional representatives.

claimed in their patent, let alone had they tried to obtain a sample of Kadcyla for testing purposes.

Genentech went on by stating that Phigenix would merely rely on unsubstantiated assumptions, and that, furthermore, the asserted claims were invalid in view of a prior art document.

Genentech asked the court to refuse Phigenix' action, plus award recompensation for disbursements Genentech had for defending the suit.

It remains to be seen how this enigmatic case turns out.

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: Ivo de Baere (IPLodge)

Ivo De Baere is a member of Euripta'a Belgian member firm, IPLodge. Ivo holds a PhD in Biology (biotechnology) from the University of Antwerp (1993) and conducted scientific research at LMB-MRC (Cambridge), Nederlands Kanker Instituut (Amsterdam) and the University of Leuven. He started his career in intellectual property in 2001, and joined IPLodge in 2013.

He has experience in the prosecution of patents of SMEs, universities, spin-offs, and multinational companies in the field of life sciences (including medical and diagnostic applications). As a result of the wide geographical coverage that is typical for patents in the medical field, Ivo is also very familiar with patent procedures outside Europe and North America.

Ivo has been a qualified European patent attorney since 2007.His professional working languages include Dutch and English. He can be reached under ivo.debaere@iplodge.be

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