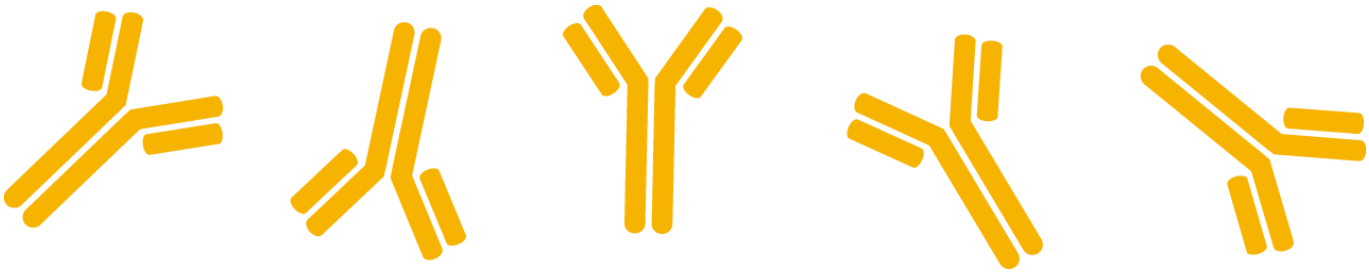

A short guide to therapeutic antibody patenting.

By Janni Wandahl Pedersen, HØIBERG A/S May 2015

Therapeutic antibodies have become an established class of drugs for the treatment of a variety of diseases, especially cancer and autoimmune/inflammatory disorders, and a sufficient patent protection is a prerequisite for their successful commercialisation.

Since the completion of the Human Genome Project, researchers developing an antibody are often faced with the situation that the target of the antibody is already known and thus cannot confer patentability to the antibody. Also, since monoclonal antibodies and their therapeutic potential have been well known for decades, the mere production of yet another therapeutic antibody is in many jurisdictions not considered a patentable invention unless the new antibody possesses novel structural features and/or improved properties that are not common to other antibodies that bind the same antigen.

Specific properties that may confer patentability to a specific antibody against a known antigen may include the following:

- Higher affinity
- Higher specificity
- Cross-reactivity with other targets or lack thereof
- Binding to a different epitope
- Higher or new pharmacological efficacy
- Fewer side effects

How to claim antibodies

Antibodies can be claimed structurally and functionally. However, most antibody patent claims include a combination of structural and functional features. In many cases there is a trade-off between structure and function in the claims. For instance, a less detailed structural definition may be accepted if combined with one or more functional features to ensure that the claim is restricted to the antibodies that actually possess the inventive function.

Antibodies are usually defined structurally in claims by reference to their amino acid sequence. For instance, an antibody may be claimed by reference to all or a part of its sequence, such as by reference to its complementarity determining regions (CDR's) or V_H and V_L domains. For instance, a structural definition of an antibody by reference to its CDR's provides flexibility for the antibody to have different framework regions.

A certain degree of structural freedom, i.e. a certain percentage of sequence identity, is usually also allowed in claims. If the claim allows for structural freedom in the variable regions of the antibody, the structural definition is normally accompanied by functional limitations to ensure that the all antibodies falling within the scope of the claim possess the inventive function.

Alternatively, it is also possible to deposit the hybridoma producing the antibody at specific depository institutions such as the American Type Culture Collection (ATCC) and directing the claims to an antibody produced by said hybridoma or an antibody comprising a part of the deposited antibody.

This option has been used less frequently in the past years because it is today common knowledge how to produce a given antibody once its sequence or the sequences of its CDRs are known. In some cases a patent application may include both an antibody sequence and a reference to a deposit as a way to make doubly sure that the antibody has been fully disclosed. If sequencing errors are discovered later,

the deposited antibody may save the day by providing an alternative way to claim the correct antibody.

Antibodies can also be defined functionally in claims based on their ability to bind to a defined epitope or by claiming antibodies that compete for binding to said epitope. Targeting a specific epitope on a known target can hypothetically result in a superior or other unexpected effect as opposed to other epitopes on the same target, thus creating the necessary basis for patentability.

Broad or narrow claims?

Often a broad patent protection is desired to ensure that the patent protects both the antibody of interest and related antibodies having the same functional features, thereby preventing competitors from marketing a functionally equivalent antibody. It is also important to keep in mind that the antibody or antibodies, which have been developed by the inventors at the time the patent application is filed, are usually altered or optimised during the course of product development, so that the final structure of the therapeutic antibody differs from the structure originally described in the patent application. When drafting the claims, care should be taken to obtain a patent scope that ensures that the patent actually covers the intended final product, which may be humanised or chimeric version of the original antibody.

Although broad patent claims are often desired, narrow patent claims essentially only protecting the antibody of interest are not without value. Such claims can effectively prevent generic companies from entering the market with a biosimilar having the same amino acid sequence as the original antibody. In addition, narrow patent claims tightly focused on a clinical candidate may also be granted more easily and be less vulnerable to post-grant attacks by competitors.

When should the first patent application be filed?

The short answer of course depends on the available resources as well as the scientific strategy of the project. It may be advisable to file a first patent application once you have sequenced your antibody (or antibodies) and performed preliminary experiments showing that the antibody performs as intended. It is then possible to follow up within the priority year with further patent applications containing additional scientific information, such as comparisons of your antibody to known antibodies or other relevant studies demonstrating the advantages of your antibody.

In any case, it is important that the patent application filed at expiry of the priority year contains experimental evidence showing the improved properties of the claimed antibody. As the generation of such evidence takes time, it may well be advisable to delay the filing of the first patent application to make sure that a sufficient amount of data can be included in the patent application upon expiry of the priority year.

Subsequent inventions relating to novel uses, formulations, dosage regimens, and combinations with other treatment modalities can be protected by further patent applications after expiry of the priority year to extend patent term.

Conclusion

It is important to focus, right from the beginning of any antibody research project, on the essential parameters that could confer superiority over the antibodies known in the art and, at the same time, could confer patentability to claims being broader than claims directed to a specific antibody itself. This involves a careful characterization of the biochemical, pharmaceutical and pharmacological properties of the antibody, preferably in comparison with known antibodies.

If you have any questions you are very welcome to contact your patent attorney at HØIBERG A/S.

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