HANNA MOORE + CURLEY

HMC-IP INTELLECTUAL PROPERTY

# Patenting Antibodies in Europe - updated EPO Guidelines for Examination

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HMC-IP attorney and EPI Biotech Committee member Anna Hally reports on the recent update to the Guidelines for Examination in the European Patent Office regarding the patenting of antibodies.

## The Rationale

Antibody-based therapeutics are now an important class of biologic therapeutics and even more so in the last year, for example, https://www.epo.org/news-events/in-focus/fighting-coronavirus/vaccines-and-therapeutics.html.

In order to facilitate increased transparency of EPO practice in this economically important sector and following EPO user input, a new section on the patenting of antibodies has been added to the Guidelines for Examination in the EPO. It is important to note that the EPO has confirmed that there has not been any change in practice. Furthermore, antibody-based therapeutics must also fulfil the same patentability requirements as for all other inventions. This new section, G-II 5.6, aims to reflect present examination practice at the EPO as it has evolved over the years in view of increasing prior art in this dynamic field.

These updates should be of particular interest to US practitioners where the approach of the EPO and USPTO to patenting antibodies differs significantly in terms of inventive step.

## New Section G-II 5.6 - The Details

The Guidelines for Examination in the EPO have recently been updated and now, for the first time, the Guidelines include an entirely new section G-II 5.6 on antibodies.

In general, antibodies (i.e., conventional antibodies, recombinant antibody derivatives or new antibody formats) can be defined in many different including structurally and/or functionally, or by production process. The EPO provides the following non-exhaustive list:

(a) their own structure (amino acid sequences);
(b) nucleic acid sequences encoding the antibody;
(c) reference to the target antigen;
(d) target antigen and further functional features;
(e) functional and structural features;
(f) the production process;
(g) the epitope; and/or
(h) the hybridoma producing the antibody.

Further details on (a) to (h) are expanded on in sections G-II 5.6.1.1 to G II 5.6.1.7 and some highlights are expanded on below.

## Definition By Structure (Sequence) Of The Antibody (a)/(b)

According to current EPO practice, a conventional antibody should be defined by **at least six Complementary Defining Regions (CDRs)**, namely 3 light chains and 3 heavy chains, to fulfil the EPO **clarity requirements of Article 84 EPC (including all essential technical features)**. There are always exceptions as outlined below:

> *'A claim to an antibody defined by its structure by fewer than six CDRs will be considered to fulfil the requirements of **Art. 84** only if it is experimentally shown that one or more of the six CDRs do not interact with the target epitope or if it concerns a specific antibody format allowing for epitope recognition by fewer CDRs.'*

## Definition By Reference To The Target Antigen or Epitope (c)/(g)

Obtaining broad protection is possible where the antibody is functionally defined by the antigen it binds to, provided the **antigen is new and clearly defined in the claims**. Examples of accepted antigen-defined antibody claim wording are:

- antibody binding to X
- anti-X antibody
- antibody reacting with X
- antibody specific for antigen X
- antibody binding to antigen X *consisting* of the sequence defined by SEQ. ID. NO: y
- antibody binding to antigen X and not binding to antigen Y

The antigen must be defined by the full sequence. Otherwise, if the antigen is not clearly defined, the EPO is likely to raise **novelty objections** over known antibodies which bind to the undefined region of the target antigen.

Where an antibody is defined by the **epitope it recognizes on the antigen**, the burden of proving that the antibody is different from prior art antibodies that bind to the same antigen but on a different epitope resides with the applicant.

In reality it is probably now more common for an invention to reside in the identification of a **new antibody for a known target**. This places a burden on a patentee to define the new antibody clearly and in such a manner it is distinguished from prior art antibodies for the same target.

## Definition By Target Antigen And Further Functional Features (d)

Antibodies may also be defined by functional features defining further properties of the antibodies, for example, the binding affinity, neutralising properties, induction of apoptosis, internalisation of receptors, inhibition or activation of receptors.

However, antibodies claimed exclusively by functional features can run into clarity objections and novelty objections over prior art disclosing (in an enabling manner) an antibody directed to the same antigen using an immunisation and screening protocol that arrives at antibodies having the claimed

properties. In this scenario, the EPO will conclude the prior-art antibody inherently displays the same functional properties as the claimed antibody, and thus lacks novelty (G-VI, 6).

In this section, the EPO remarks that where an antibody is defined exclusively by functional properties, the application must provide an **enabling disclosure across the whole scope claimed** (Article 83 EPC Sufficiency) and the EPO will assess whether the functional definition allows the skilled person to clearly determine the limits of the claim (Article 84 EPC Clarity).

## Definition By Functional And Structural Features (e)

Due to the inherent risks of defining by functional features alone, a better compromise is to define the antibody with a combination of structural and functional features. In this manner, it is possible to claim an antibody characterised by the sequences of both variable domains or CDRs **with less than 100% sequence identity when combined with a clear functional feature**.

Finally, as outlined in G-II 5.6.1.5 & 7, **antibodies may also be defined by the process of their production or by hybridoma cell line producing the antibodies** ((f)/(h)).

## Inventive Step

Once the EPO has confirmed that a further antibody binding to a known antigen is novel, an inventive step will only be acknowledged if a **surprising technical effect** is shown by the application.

The EPO approach in this field is that the **generation of an antibody to a known antigen merely involves routine experimentation**. As such, additional proof is required by the EPO to establish the required surprising technical effect. Examples of a surprising technical effect include:

- an improved affinity;
- an improved therapeutic activity;
- a reduced toxicity or immunogenicity; and/or
- an unexpected species cross-reactivity or a new type of antibody format with proven binding activity.

It is also important to note that

> *'If inventive step relies on an* improved property versus the enabled antibodies of the prior art, ***the main characteristics of the method for determining the property must also be indicated in the claim or indicated by reference to the description*** *(F-IV, 4.11.1).'*

This surprising technical effect is ideally shown compared to 'enabled antibodies of the prior art' i.e., known/prior art antibodies to the same target. One question that has not been addressed (and will also be case specific) is the extent of the data required in the description to support this surprising effect.

For these reasons, arriving at alternative antibodies by applying techniques known in the art is considered by the EPO to be obvious to the skilled person. The fact that the structure of the alternative antibodies, i.e., their amino acid sequences, is not predictable is not a reason for considering these antibodies as non-obvious. In essence, at the **EPO structural non-obviousness, or unpredictability, does not support an inventive step** of a novel antibody binding to the same antigen as known antibodies. Thus, for the EPO to acknowledge an inventive step, experimental

evidence will be required to demonstrate this surprising technical effect. This is one of the major differences between USPTO and EPO practice.

Despite this, it should be noted that antibodies can be inventive if the application overcomes technical difficulties in producing or manufacturing the claimed antibodies.

## Take Home Advice

It is expected that this new Guidelines section will evolve over time and our advice when drafting patent specifications concerning antibody based therapeutics is to include as many fall back positions as possible, particularly when relying on functional features to define the antibody.

In general, broadly worded antibody claims can run into problems at the EPO in terms of clarity and novelty over prior art that is potentially yet to be identified. Thus, we would recommend including a combination of definitions (a) to (h) as fallback features in the specification.

In terms of inventive step, filing a patent application in the early research stages with only structural information available can be a risky approach at the EPO. Thus, consideration should be given at the time of filing a patent application, as to whether some initial supporting data can be included in the application as filed along (noting that additional experimental data may also be filed during downstream prosecution).

Please contact the author or one of our HMC-IP attorney team for further advice.

**AUTHOR**
**ANNA HALLY**
European + UK Patent Attorney

Direct: +353 1 618 1916
Email: ahally@hmc-ip.com

For any specific concerns, contact the author or any one of our European Patent and Trade Mark Attorney team at Hanna Moore + Curley.
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HANNA MOORE + CURLEY
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**Ireland, UK, and China**

Garryard House,
25/26 Earlsfort Terrace,
Dublin 2,
D02 PX51, Ireland
Tel: +353 1 661 3930
Fax: +353 1 661 3453
Email: mail@hmc-ip.com

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MIP IP STARS TOP TIER FIRM
iam 1000