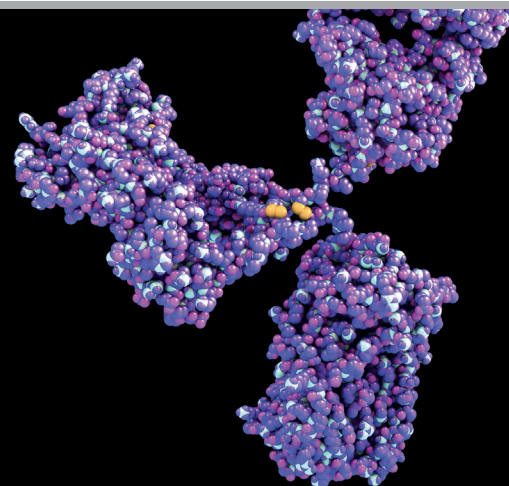


Patenting across three jurisdictions

There are a number of key differences between the US, Canada and Europe when patenting antibodies



During the past 35 years, around 100 monoclonal antibodies have been designed as drugs to treat various diseases.¹

US

In the US antibody claims must satisfy the requirements under 35 USC sections 101 (statutory subject matter), 102 (novelty), 103 (obviousness), and 112 (written description and enablement). The tricky hurdle to overcome when patenting antibodies is section 112. Importantly, the US requirements for patenting antibodies have changed recently, with the Federal Circuit overturning the newly characterised antigen test.

This test was originally adopted by the Federal Circuit in 2002.² Under it, claims directed to antibodies would meet the requirements of section 112 so long as there was disclosure of the structure of the antigen to which the antibodies could bind; and disclosure of routine methods of making the antibodies capable of binding the antigen. For over 15 years, the US Patent and Trademark Office tended to issue broad genus claims to antibodies under this test.

In 2017 the landscape for patenting monoclonal antibodies (MAbs) in the US changed when the Federal Circuit overturned the newly characterised antigen test in *Amgen v Sanofi*.³ The court reasoned that the test permitted broad genus claims to antibodies without satisfying the written description requirement under section 112. The court stated that the newly characterised antigen test “flouts basic legal principles of the written description requirement” by allowing “patentees to claim antibodies by describing something that is not the invention, ie, the antigen”.⁴

Accordingly, after *Amgen v Sanofi* antibody genus claims should be drafted to satisfy the same written description standard as any other chemical genus. In other words, a patent application for broad antibody genus claims should include either a representative number of species that make up the genus or structural features that are common to the genus of antibodies.⁵

To meet these requirements, applications should include as much structural information as possible about the claimed antibodies instead of relying on the function of an antibody genus to bind to a specific antigen/epitope. Such structural information includes amino acid sequences for the variable regions and/or complementary-determining regions (CDRs) of the antibodies, or consensus sequences on the antibodies critical at the antibody/epitope-binding interface.

Canada

Antibody claims must be directed to patentable subject matter that is novel, non-obvious, supported by an enabling written description, and be either demonstrated or soundly predicted to have utility.⁶

An important difference compared to the US is that Canadian patent law considers an isolated antibody obtained from a natural

source to be patentable subject matter, even if the antibody is defined by an amino acid sequence (or its corresponding DNA sequence) that is identical to the antibody sequence found in nature.

Additionally, Canada, unlike the US, permits claiming an antibody by defining an antigen that can be used to produce it. As in the US newly characterised antigen test, to be novel the antigen must not have been previously characterised. To help meet the requirements for an enabling description, the patent application should be drafted to include evidence that it would only require non-inventive methods to produce an antibody without requiring significant trial and error experimentation. That being said, PTAB decisions have allowed claims directed to chimeric antibodies⁷ as well as humanised antibodies^{8,9} based on a fully characterised target antigen.

“A patent application for broad antibody genus claims should include either a representative number of species that make up the genus or structural features that are common to the genus of antibodies.”

An antibody can also be claimed based on a characterisation of the epitope. Even where the epitope forms part of an antigen that was previously characterised, a claim defining an antibody by its cognate epitope may be novel and non-obvious so long as the epitope would not have been accessible to bind and activate antibody-producing B cells. This should be included in a patent application, when available, to assist in meeting novelty and enabling description requirements.

A common antibody claim is one that defines the variable region of the antibody by specifying the CDRs that define the antigen-binding site. In many situations, the claims will have to specify the CDR amino acid sequences to show novelty and non-obviousness when the cognate antigen was characterised in the prior art, or when an alternative antibody for the antigen was previously described. In the absence of evidence to the contrary, the Canadian Intellectual Property Office (CIPO) will assume that all six CDR sequences are essential for binding to the epitope. This assumption may not be fair as not all CDRs necessarily contribute equally to binding the epitope.

Furthermore, there are examples in which only the heavy chain is required for antigen binding. As such, written description and evidence demonstrating that fewer than six CDRs are sufficient for epitope-binding should be included in an application, when available, to provide an enabling description for fewer than six CDRs and to support a sound

prediction that all members of the claimed antibody genus would have utility in binding the intended antigen.

Similarly, available evidence that certain amino acids in the CDR sequences may be substituted without abrogating epitope-binding should be included in the application. Otherwise, the CIPO will find any deviation from the exact CDR sequences to be not-enabled by the description or to define a genus of antibodies that are not soundly predicted to have the intended epitope-binding utility.

Claims may also specify a particular functional feature of an antibody beyond mere specific binding to a particular antigen/epitope – eg, a particular level of binding affinity, selective binding to a particular epitope within a larger antigen, agonist activity or antagonist activity, or therapeutic activity. Inclusion of such claim features will trigger the CIPO to look for additional written description and evidence to satisfy the enabling description and utility requirements, and care should therefore be taken to include information/evidence appropriate to the common general knowledge available at the application filing date.

Europe

Antibody claims must meet the requirements of novelty (Art 54 EPC), inventive step (Art 56 EPC), enablement (Art 84 EPC) and clarity (Art 84 EPC).

Like Canada, the European Patent Office (EPO) permits claims to antibodies that are characterised only by their ability to bind a novel antigen even if not supported by antibody data. The reasoning behind this is that a claim to such an antibody is by definition novel and inventive and also meets the requirements of Article 83 EPC, as generating an antibody against a previously disclosed antigen is not an undue burden.¹⁰

Consequently, once a protein belongs to the state of the art, an antibody defined merely by its ability to bind to it will not be considered inventive, unless it can be demonstrated that obtaining the antibody was unexpected, eg, as a result of the exceptional nature of the protein.¹¹ Contrary to the US, such a lack of inventive step objection cannot be remedied or avoided if the claim is limited to a specific antibody as the EPO does not consider a novel antibody inventive *per se*.¹²

An antibody claim directed against a known antigen will only be considered inventive if the antibody has an unexpected property or effect. While introducing this as a functional feature will ensure the broadest claim scope, some hurdles will still have to be overcome. The first is demonstrating novelty over prior art antibodies against the same target, which may not have been tested on this feature. In this regard, similar to the CIPO, the EPO will allow claims to an antibody characterised by its binding to an epitope with an unexpected effect, though the burden of demonstrating the difference with the prior art antibodies is with the applicant.¹³

The EPO has become more critical of the inventiveness of functional features in antibody claims. Similarly, claims will no longer be allowed merely because the antibody is chimeric, humanised or human.¹⁴ Where a functional feature is considered unexpected, whether the claim meets the requirement of Article 83 EPC may be questioned because the application must disclose how additional antibodies that have this unexpected feature can be obtained. If the description suggests that the functional feature claimed is linked to a specific structural property, claiming the structural feature may be required under the premise that, in its absence, the problem is not solved over the entire scope of the claim.

If the introduction of structural features is required, this will typically require the introduction of the sequence of at least the six CDRs, unless data are provided to support a broader claim.¹⁵ The combination of a functional feature and a partial structural limitation has been considered to address both inventive step and enablement issues.¹⁶

Finally, the EPO will more easily allow a functionally defined antibody where the inventive contribution of the claim lies in the application of the antibody, such as in first or second medical use claims or *in vitro* diagnostic claims, provided that it is considered plausible that the technical effect can be obtained over the entire scope of the claim.¹⁷

Summary

While there are common features required in all three jurisdictions for successfully patenting antibodies, this article outlines a number of key differences. Companies and institutions that develop and produce antibodies are wise to reach out to foreign counsel early in the patent process.

Footnotes

1. See online: <https://www.uptodate.com/contents/overview-of-therapeutic-mono-clonal-antibodies>
2. *Enzo Biochem, Inc v Gen-Probe, Inc*, 323 F.3d 956 (Fed Cir 2002).
3. *Amgen Inc v Sanofi*, 872 F.3d 1367 (Fed Cir 2017).
4. *Id* at 1378.
5. *Regents of Univ of California v Eli Lilly and Co*, 119 F.3d 1559 (Fed Cir 1997).
6. Patentable subject matter and utility are required under s 2 of the Patent Act, RSC, 1985, c P-4. Novelty and obviousness are required under ss 28.2 and 28.3 of the Patent Act, respectively. Support and sufficient written description are required under s 27(3) of the Patent Act and s 60 of the Patent Rules, SOR/2019-251.
7. *Re Sloan-Kettering Institute for Cancer Research*, Patent Application No 2,072,017 (CD 1296)
8. *Re Immunex Corporation*, Canadian Patent Application No 583,988 (CD 1302)
9. *Re Chugai Seiyaku and Kabushiki Kaisha*, Canadian Patent Application No 2,451,493 (CD 1398)
10. Board of Appeal Case T877/03.
11. Board of Appeal Case T0187/04.
12. Board of Appeal Case T735/00.
13. Board of Appeal Case T735/00.
14. Board of Appeal Case T0782/07.
15. Board of Appeal Case T511/14.
16. Board of Appeal Cases T418/07 and T617/07.
17. See EP1591527 (Ono Pharmaceutical Co Ltd)

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