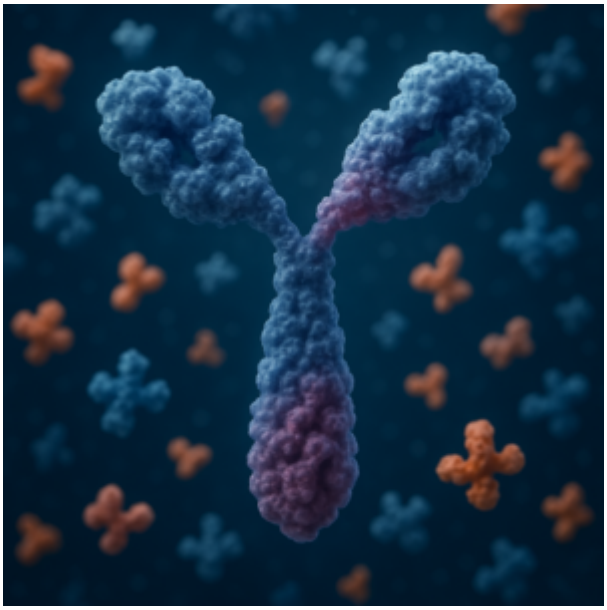
Kluwer Patent Blog

Epitope claims are still alive at the EPO

Adam Lacy, Irene Martin Badajoz (Hoffmann Eitle) · Wednesday, June 11th, 2025

Defining antibodies by functional features is not always straightforward at the EPO. **T326/22** is a nice example of how this can be achieved.?

? 

To briefly recap the standard EPO approach, an antibody may generally be claimed by reference to its epitope, i.e. the structurally defined part of the antigen that it specifically binds to (G, II, 6.1.3). ?In these cases, the application must enable the skilled person to produce further antibodies having the claimed functional property without undue burden. ?In addition, unless the application shows a surprising technical effect or there was no reasonable expectation of success in obtaining antibodies having the required properties, the inventive step requirement will not be acknowledged (G, II, 6.2). ?In practice, defining antibodies by their binding epitope is not always straightforward.?

?

The antibodies claimed in claim 1 of AR1 in?the application underlying T326/22 encompassed a pool of antibodies for human cell surface protein CD47 that were functionally defined only.? Claim 1 was directed to an isolated monoclonal antibody (mAb) (full-length or fragments thereof) defined by the following functional features:?

?

(i) it **binds** to a discontinuous **epitope** on human CD47, which?**comprises?amino acids residues**?Y37, K39, K41, K43, G44, R45, D46, D51, H90, N93, E97, T99, E104, and E106 of CD47 when numbered in accordance with SEQ ID NO: 147;?

(ii) it **prevents CD47 from interacting with**?signal-regulatory-protein a (**SIRP?**); and?

(iii) it does **not cause a significant level of agglutination**?of cells after administration.?

??

The epitope (i) to which the claimed mAb or fragment thereof binds must comprise the cited amino acids, but the epitope is not limited thereto. ?Further functional requirements (ii) and (iii) are not further defined in the claim, e.g., by reference to a certain level/degree, mAb concentration or a reference CD47 Ab. ?It was not contested by the parties that requirements (ii) and (iii) result from the antibodies' binding to the epitope on CD47 as defined in (i), and not from their constant regions.? Therefore, the binding of an antibody to the claimed epitope must be such as to fulfil the two other properties mentioned ((ii) and (iii)), and this?**depends on the antibody's orientation on CD47 when bound to the claimed epitope**.?

??

The patent provided sequence information for a **single antibody** (2A1) and its derivatives.? The Board concluded that the claim was reproducible over its entire scope and that the patent as maintained by the Opposition Division complied with the requirements of Art. 83?EPC.? For the Board's conclusion it was decisive that the patent described the generation of at least one mAb falling within the scope of the claim, i.e., antibody 2A1.? It was decisive that the patent provided the **antigen** used for immunization and the **assays** relied on for screening and selecting SIRP?-blocking for (ii) and non-cell agglutinating CD47 antibodies for (iii).? Further, the patent also provided means (X-ray crystallography) for determining the epitope structure on CD47 bound by the chimeric antibody 2A1 and disclosed the **epitope's structural information**.? Finally, the patent taught that a **cross-competitive binding assay** may be used to test the candidate antibodies for their binding to 2A1's epitope on CD47.?

?

The discussion on inventive step focused on whether the binding to the specific epitope was associated with any technical effect which exceeds the mere provision of antibodies against a further (**arbitrary**) epitope on a known antigen (CD47).? The Board was convinced that the two functional features (ii) and (iii) of the claimed antibodies were a direct consequence of the epitope they bind to.? In other words, the Board was convinced (and it was uncontested) that any antibody binding to the claimed epitope has a non-significant cell agglutinating and a SIRP?-blocking activity.???

?

Starting from **D1** (which disclosed an anti-CD47 full-length antibody), the problem was formulated as the provision of **improved** antibodies.? In particular, the Board was convinced that all antibody embodiments falling within the scope of claim 1 show less cell agglutination compared to the full-length monospecific and bispecific antibodies of **D1**. The claimed solution was considered inventive as none of the cited documents pointed towards the epitope of claim 1.??

?

An alternative starting point, **D13**, disclosed anti-CD47 **antibody fragments** which lack hemagglutinating activity. ?The only difference with the claimed antibodies was thus the binding epitope, and the problem was formulated as the provision of **alternative** CD47 antibodies or fragments thereof. ?The Board took the position that the selection of the claimed epitope was still **not arbitrary**, since it allowed the skilled person?a **free choice as regards the CD47 antibody format** (full-length or fragments thereof) for any intended application. **D13** in contrast disclosed that the epitope bound by the anti-CD47 antibodies imposed different functional properties on these antibodies depending on their format: full-length antibodies agglutinated cells, so it did not achieve (ii) – only the fragments achieved (ii). Since none of the documents pointed to the specific claimed epitope for removing any potential restrictions as regards the format of the antibody, the Board concluded that the skilled person would also not arrive in an obvious manner at this epitope.?

??

This decision confirms that antibodies defined by their binding epitope can still be patented in Europe.? Applications directed to antibodies defined by their binding epitope should provide the skilled person with enough guidance enabling him or her to generate antibodies falling within the scope of the claim, e.g., the exact epitope used for immunizations, specific screening assays, how to structurally characterize the binding epitope, etc.? In addition, the choice of epitope should not be arbitrary; functional features specifically linked to the binding epitope should be well characterized and, if possible, comparative data with antibodies binding to different epitopes, provided.? This decision provides with further tools for defending the sufficiency and inventive step of antibody claims which can be added to the ones proposed by Tamaris Bucher and discussed by Brian Cordery here: The approach to the assessment of inventive step of antibodies at the EPO – is there an artificial barrier and should it be broken?

This entry was posted on Wednesday, June 11th, 2025 at 5:20 pm and is filed under Antibodies, Biologics, EPC, EPO, EPO Decision, Inventive step, Opposition, Patents
You can follow any responses to this entry through the Comments (RSS) feed. You can leave a response, or trackback from your own site.