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Antibody Appeals Uncovered

A High-Level Analysis of EPO Decisions

July 2024

Since the first approval of Muromonab-CD3 in 1986, antibodies have become progressively more common, frequently reaching a 'blockbuster' status. According to statistics provided by Statista in March, 5 out of 10 top-selling drugs were antibodies in 2023[1]. Therefore, patents related to antibodies are now of considerable interest and significance to the pharmaceutical industry. They provide protection for commercially important inventions, spur further investment, and allow patients to benefit from these therapeutics.

In Europe, the interest in patents related to antibodies led to the development of a body of case law by the Boards of Appeal (BoA) of the European Patent Office (EPO). A lot can be learned from the detailed reasoning in BoA decisions. However, a higher-level analysis of the BoA decisions in this technical area can also help to identify any notable trends and other useful information.

As a first step, this article presents data collected by CMS from BoA decisions between 2017-2023 based on appeals from the Opposition Division (OD) for antibody-related patents.

Surprisingly, our analysis highlights differences between the outcomes of appeals related to antibodies and other areas of technology. Our data suggests that, for antibody[2] and reference[3] cases alike, the BoA is often inclined to deviate from the first instance decision of the OD. In many cases, this leaves patentees in a worse position and can create a level of uncertainty following opposition. The differences between the antibody-related appeals and the reference set are the most pronounced following a first instance opposition rejection. Additionally, we identify differences in the reasons for main request rejections between the two datasets.[4]

Throughout the last few years, there have been a number of amendments to the EPO's Guidelines on patenting antibodies. Major changes to the Guidelines came about in 2021 and more recently in 2024 the Guidelines were amended further. It is paramount that applicants carefully consider the developing case law relating to antibodies, specifically on the EPOs practice on inventive step and sufficiency. These matters are characterised by EPO-specific considerations, with potentially deleterious consequences for applicants if not considered during the drafting and prosecution of antibody-related applications at the EPO.

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[1] https://www.statista.com/statistics/258022/top-10-pharmaceutical-products-by-global-sales-2011/ Accessed: 8 April 2024

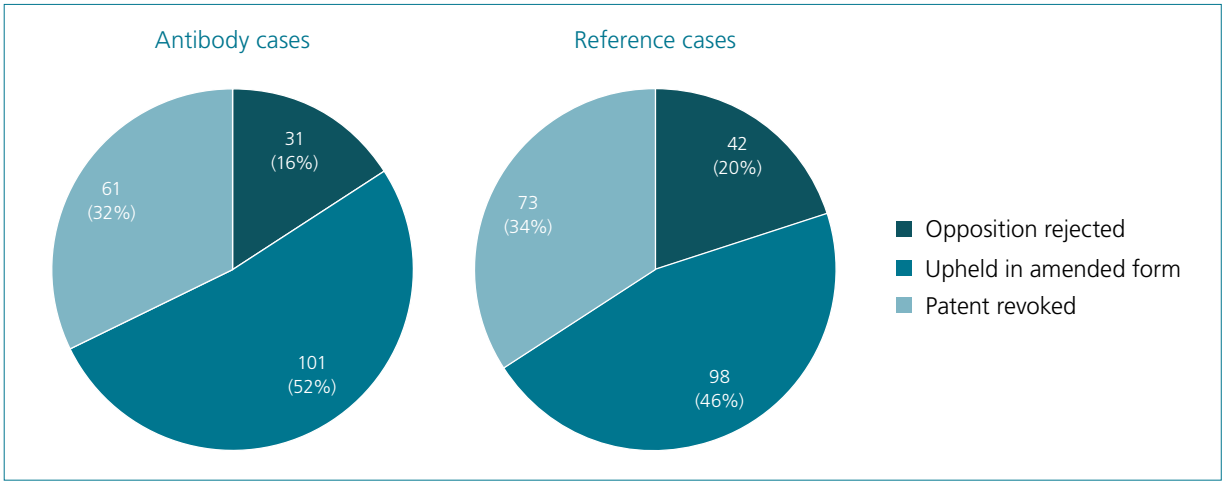
[2] The dataset of antibody-related patents was generated using a search of the EPO BoA decisions database, using the search term 'antibod' in the full text search field. Decisions forming this dataset were limited to English language decisions and based on appeals from OD decisions. It should be noted that some decisions are made available online many months into the next year; for completeness, it is therefore noted that the antibody dataset is correct as of 9 April 2024.

[3] The dataset of reference cases was generated using the same search criteria as for the antibody cases dataset, but without the search term 'antibod' and limited to BoA 3.3.01, 3.3.04 and 3.3.08. Only decisions issued by these BoA were included as these were the BoA most often dealing with cases in the antibody cases dataset. The reference cases dataset consists of a similar number of reference cases per year as the antibody cases. Any cases in which the BoA did not decide on the patentability of any claim requests where excluded from the search results.

[4] It will be appreciated that the datasets in this analysis and the absolute numbers are relatively small. As a result, observed results and trends may not be fully representative at this stage.

Opponents advantage: Opposition outcomes lean towards amendment or revocation at 1st instance

Figure 1. The proportion of outcomes of first instance decisions that are appealed in antibody-related cases (left hand chart) and reference cases (right-hand chart). A higher proportion of antibody cases end in amendment, compared to reference cases.



At first instance, **only about 16%** of opposed patents were **maintained as granted** by the Opposition Division. **Around 84%** of oppositions result **in the revocation or amendment** of an antibody patent by the Opposition Division.

A higher proportion of antibody patents were **upheld in amended form** (52% for antibodies as compared to 46% for reference). There are correspondingly fewer of the other two first instance decisions in the reference case data set.

This may indicate that the Opposition Division believes Examining Divisions are granting **broader claims for antibodies** than for other similar technologies but that antibody patents are therefore **easier to 'salvage'** by amendment.

However, from the data above it is clear that in most instances **(over 80%)** an opposition against an antibody patent or any other similar type of technology results in either amendment of revocation of the patent.

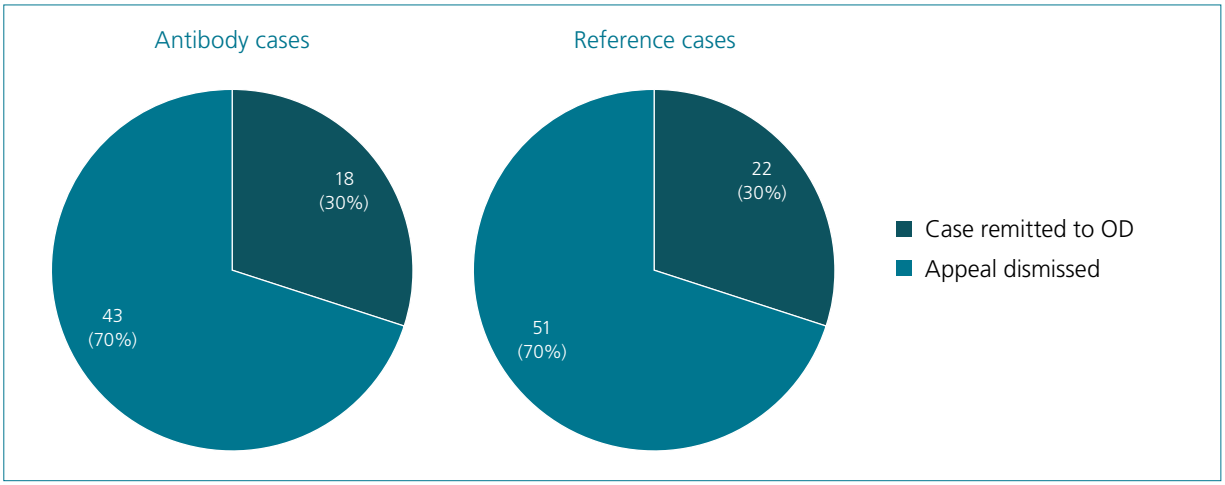
Interestingly, the EPO annual report 2022 shows slightly higher proportions of both opposition rejections and patent revocations when compared to both antibody and reference datasets. Amendment following opposition constituted a lower proportion (around 33%) of OD decisions in the EPO dataset covering all technologies.

From the data above it is clear that in most instances (over 80%) an opposition against an antibody patent or any other similar type of technology results in either amendment of revocation of the patent.

Appeal after revocation: A glimmer of hope for patentees but a beacon of hope for opponents

According to the EPO's annual report 2022, around 40% of opposition outcomes are appealed. But what is the likelihood of salvaging an antibody-related patent following **revocation at first instance?**

Figure 2. The proportion of antibody cases (left-hand chart) and reference cases (right-hand chart) following revocation of a patent at first instance which end in case remittal and dismissal of the appeal.



The **vast majority** (~70%) of revoked antibody patents **remained revoked** after appeal. However, in around 30% of appeals following a revocation of an antibody patent, the case was remitted to the OD.

There were no differences in the proportion of cases remitted by the BoA between the antibody and the reference cases.

The above data indicate that **the majority** of antibody and non-antibody patents which are revoked at first instance **stay revoked after appeal**. There is no evidence in the data to suggest any differences between antibody patents and other patents assessed by the same BoAs. This may suggest that in the majority of cases, the BoA agrees with the OD's decisions to revoke patents in both antibody and non-antibody cases.

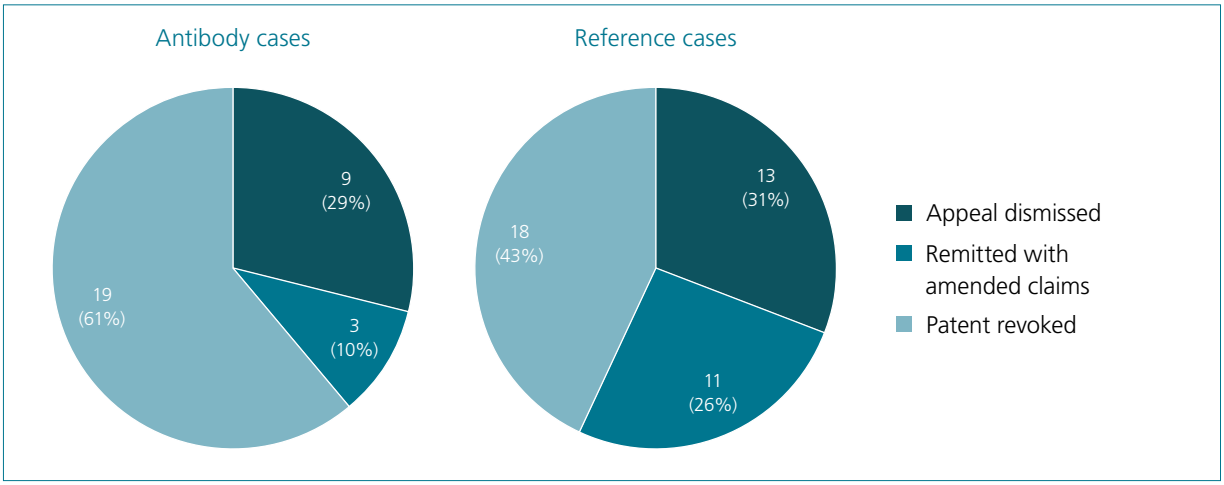
Moreover, when these data are combined with the data concerning the number of antibody patents revoked at first instance, we see that around **22% of opposed antibody-related patents are revoked at first instance and remain revoked after appeal**.

On one hand, the data indicates that even though opponents are generally in a more favourable position during an appeal by the patentee following a patent revocation, they cannot be complacent. Conversely, the patentee should carefully consider appealing the revocation as for 30% of patent revocations were nevertheless overturned and case remitted.

According to the EPO's annual report 2022, around 40% of opposition outcomes are appealed.

First instance opposition rejections: the illusion of safety for patentees

Figure 3. The proportion of antibody (left-hand chart) and reference (right-hand chart) appeal cases which end in revocation, amendment or dismissal of the appeal following a rejected opposition.



When an antibody patent was maintained as granted and appealed by the opponent, the patent was **revoked** by the BoA in **61%** of cases.

In **only about 29%** of cases, the Opposition Division's decision to **maintain the patent as granted** was upheld on appeal.

It appears that a first instance decision resulting in rejection of an opposition may create an illusion of safety for the patentee in a surprising majority of cases.

For reference cases, there was a more **even split** between the appeal being dismissed (and therefore the patent being maintained as granted), limitation of the claims, and revocation of the patent. Accordingly, there was a **much higher proportion of appeals being remitted with amended claims** in the reference cases when compared to the antibody cases.

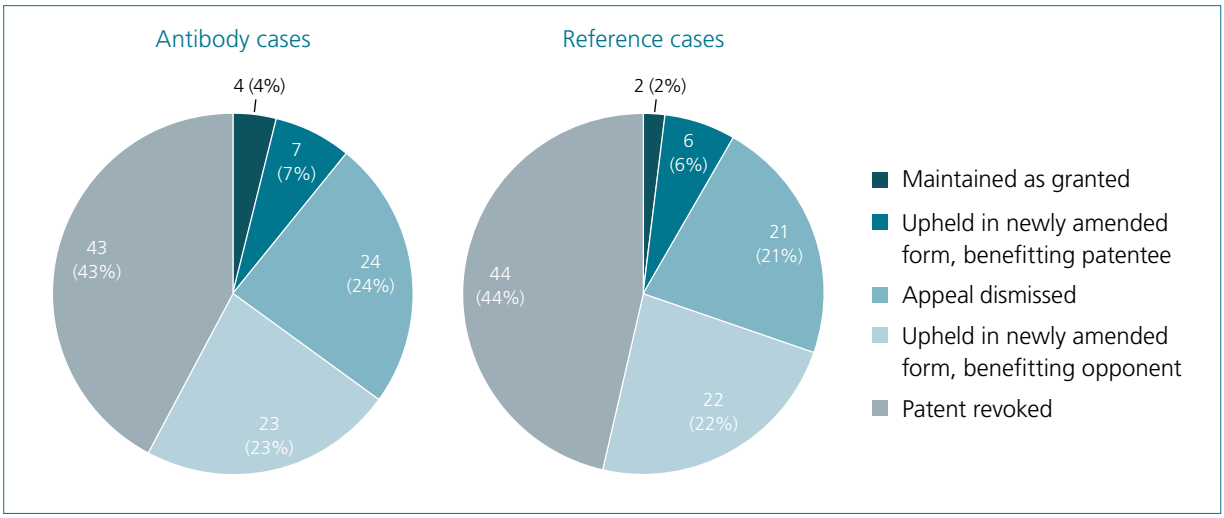
On average, **only 5%** of opposed and appealed antibody-related patents are **maintained as granted at opposition and remain as granted after appeal**, highlighting the importance of EPO opposition proceedings to applicants and opponents alike.

Antibody-related patents were 17% more likely to be revoked on appeal following a rejected opposition compared to the reference. Overall, and somewhat surprisingly, appeals following rejection of the opposition appear to favour the opponent in both antibody and reference appeals. However, antibody-related appeals were more likely to end in revocation. This demonstrates the actively developing area of case law with regards to the antibodies, as the OD decisions to reject the opposition were overturned in 70% of the antibody-related appeals.

There could be numerous reasons for the increased proportion of revocations following a first instance opposition dismissal seen in antibody-related patents compared to non-antibody patents. We later report a higher number of main request rejections on the grounds of sufficiency seen in antibody-related patents compared to reference cases. As established in the Enlarged Board of Appeal decision of March 2023 (G2/21), post-filed data may be considered to support an inventive step but cannot be used to rectify insufficiency since this is assessed at the priority/filing date. Therefore, it may be more difficult to rescue a patent opposed/appealed on the ground of insufficiency. The higher proportion of sufficiency-based main request rejections seen in antibody-related cases may partially explain the higher proportion of revocations observed above.

But what about patents amended at first instance?

Figure 4. The proportion of antibody-related (left-hand chart) and reference (right-hand chart) appeals which end in maintenance of the claims as granted; claim amendment benefiting the patentee; dismissal of the appeal; amendment benefitting the opponent and revocation.[5]



65% of antibody-related appeals resulted in a **better** situation **for the opponent**, when comparing the 1st instance decision with the appeal decision. In particular, a large proportion of these patents were **revoked**.

In **24%** of cases, the **BoA agreed** with the amended claims upheld by the OD.

In only **11%** of cases was the outcome more **beneficial for the patentee** after appeal.

The spread seen for antibody patents **broadly matches** those for the reference cases.

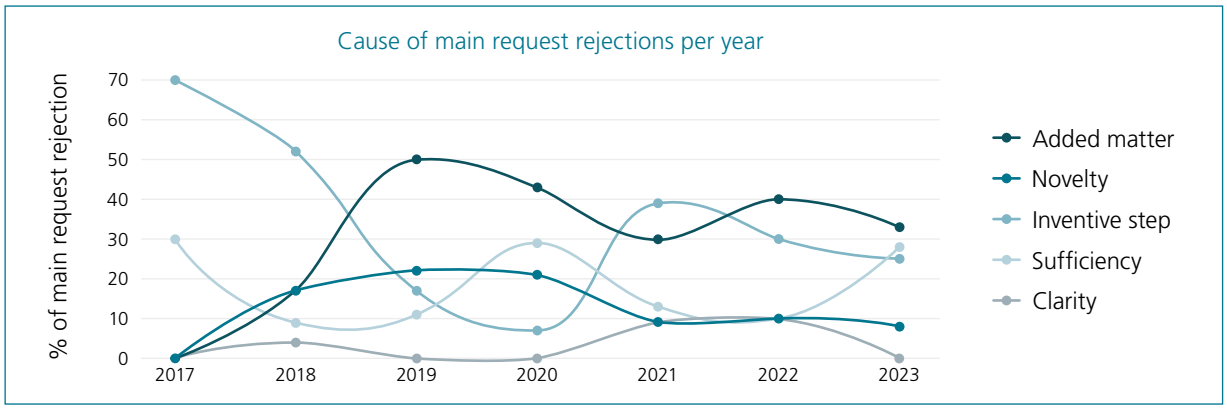
Thus, the general trend that appeals most frequently end with a decision which benefits the opponent can also be seen when it comes to appeals following the OD upholding a patent in amended form. In both antibody-related cases and reference cases, around 60% of BoA decisions resulted in an outcome which benefitted the opponent. Therefore, patentees should not be complacent if an opposition is originally rejected or upheld in amended form.

In both antibody-related cases and reference cases, around 60% of BoA decisions resulted in an outcome which benefitted the opponent.

[5] We make the following assumptions to determine whether the appeal favours the patentee/the opponent. First, we assume that when only one side appeals (the patentee/the opponent(s)), when appeal is allowed the result must be beneficial to that party. Second, where both sides appeal, we assume that unless the patentee's main request submitted with the grounds of appeal is allowed, the result is beneficial to the opponent.

Why are main requests rejected?

Figure 5. The percentage of main request rejections based on the different grounds of appeal for antibody cases.

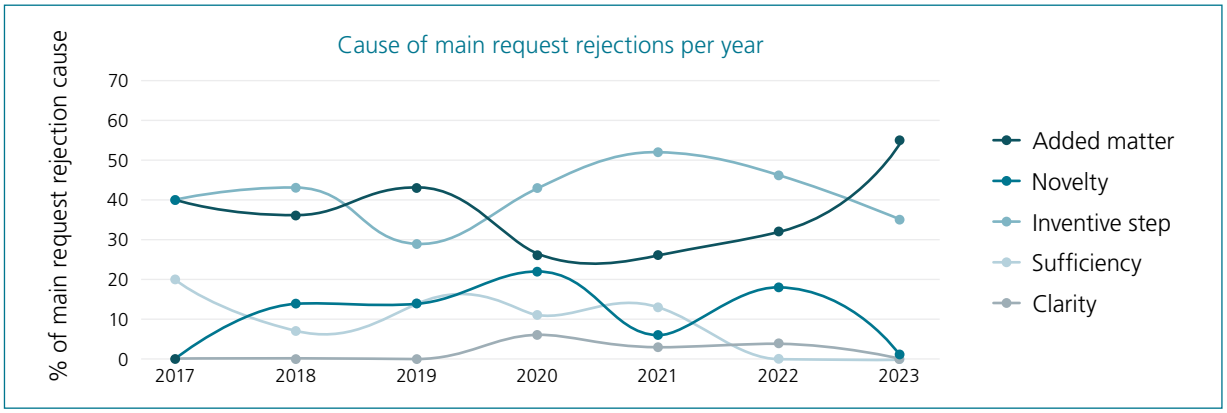


Since 2017, there has been a sharp rise in the proportion of main requests rejected on the grounds **of added matter, which accounted for 33% in 2023**.

Main request rejections on the ground of **sufficiency** have fluctuated over the years, and also accounted for **33% of rejections in 2023**. Moreover, inventive step rejections seem to have decreased over time, accounting for 25% of main request rejections last year. Novelty and clarity were the least common grounds for main request rejections.

Clarity is not a ground for rejection that is generally available in opposition proceedings unless the claims have been amended and so, not unsurprisingly, this ground is the least frequent ground for rejection of a main request.

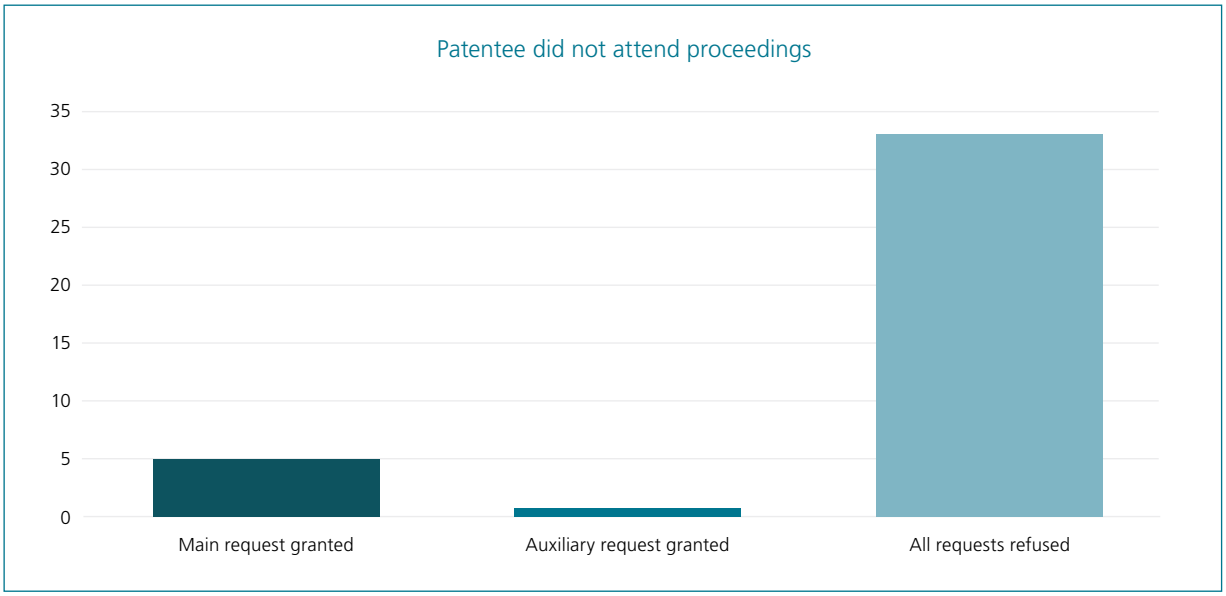
Figure 6. The percentage of main request rejections based on the different grounds of appeal for reference cases.



For reference cases, **inventive step and added matter have been the most frequent grounds** of main request rejections since 2017. Therefore, the rise in added matter rejections seen in antibody-related appeals puts antibody appeal outcomes **in line with reference** appeal outcomes. However, the reference cases do differ from antibody-related cases in that added matter and inventive step are consistently and by far the most common causes for rejection of main requests in the reference cases. This distinction is not quite as clear in the antibody-related cases, where sufficiency-based decision are more abundant.

Why you should attend oral proceedings

Figure 7. The outcomes of antibody and reference cases when patentees do not attend oral proceedings. Data are presented as absolute numbers.



The data presented combines both antibody and reference cases due to the relatively low number of antibody appeals where the patentee did not attend the oral proceedings. Regardless of whether the opponent attended, **all requests were refused** in **85%** of cases where the patentee did not attend oral proceedings.

Therefore, from the available data, it would appear that patentees should attend oral proceedings if possible. It is likely that non-attendance may result in refusal of the main or auxiliary requests. This may be because non-attendance to oral proceedings takes away a patentee's opportunity to argue their case on the day which may lead to refusal of the main and auxiliary requests. However, it could also be true that patentees are less inclined to attend oral proceedings when it appears likely that all requests will be refused, for example after a negative preliminary opinion.

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Practical Takeaways

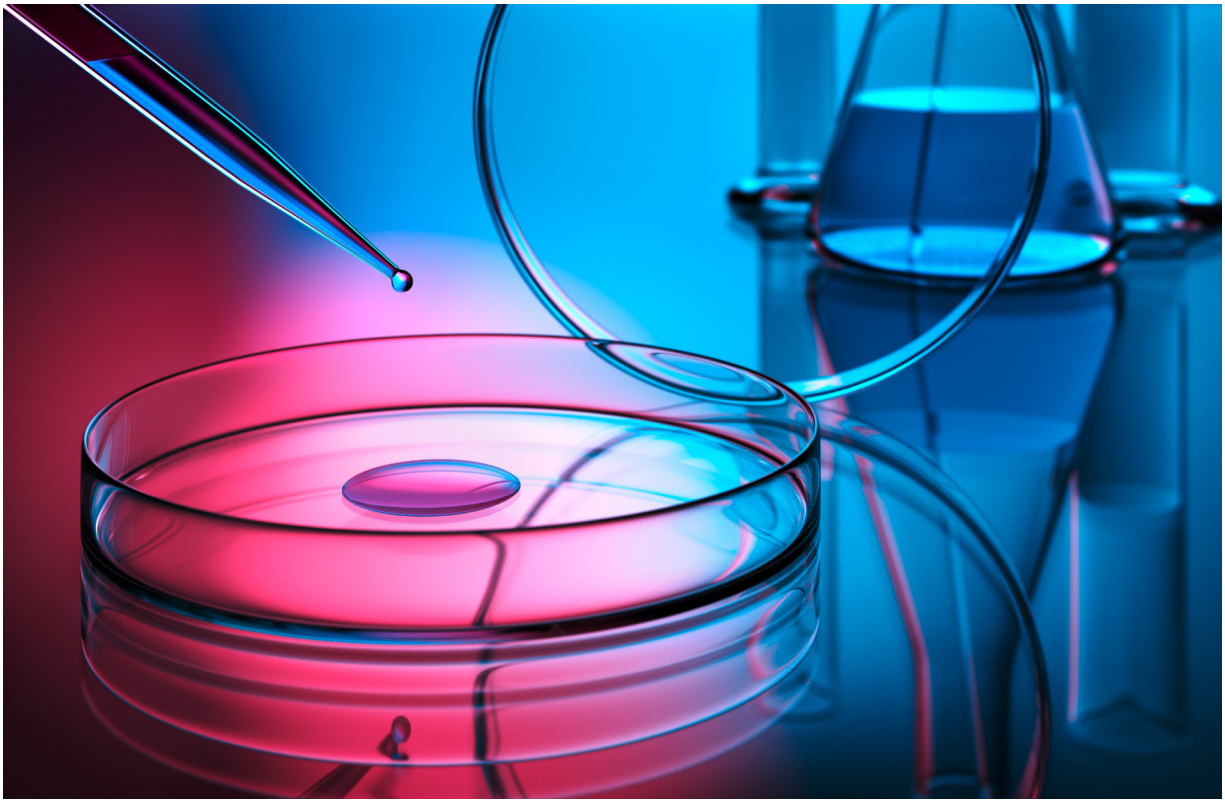
From the data above, a thorough understanding of the EPC and EPO case law and Guidelines, particularly concerning added-matter, inventive step and sufficiency is invaluable when seeking to obtain EP patent protection for an antibody-related technology.

Added Matter

Those familiar with the EPO's strict practice on added matter may not be surprised by the seemingly high proportion of main request rejections on that ground. Once again, this confirms the importance of working closely with your European patent attorney when drafting the specification and later when deciding on amendments. Patentees should take great care to avoid the 'inescapable trap' in opposition whereby an amendment in a claim is found to add matter but cannot be removed from the claim since it would impermissibly extend the scope of protection – thereby inevitably resulting in revocation.

Inventive Step

An understanding of the intricacies of the EPO-specific problem solution approach and the case law surrounding inventive step and post-published data is crucial. This includes the Enlarged Board of Appeal decision of March 2023 (G2/21), concerning technical effects "encompassed by the technical teaching" and "embodied by the same originally disclosed invention". Moreover, when drafting and prosecuting an antibody application at the EPO, it is also important to understand the EPO Guidelines and provide examples of unexpected technical effects (EPO Guidelines Chapter II 6.2) that can be used as the basis for an inventive step



argument for antibody-related cases. This is to ensure that potential unexpected technical effects are "conceptually comprised by the broadest technical teaching of the application as filed" and that the skilled person, having the common general knowledge on the filing date in mind, and based on the application as filed, would not have "legitimate reason to doubt that the purported technical effect can be achieved with the claimed subject-matter" (T116/18).

Effectively deploying arguments around lack of a reasonable expectation of success can also be successful for patentees in both prosecution and in appeal.[6]

Sufficiency

Looking at the high proportion of the sufficiency-based rejections for antibody-related appeals, at the time of drafting, careful consideration should be given to the data included to provide support of an invention. This is particularly important for any purpose-limited product claims where the application must credibly show that the claimed therapeutic use is achieved. As confirmed by the Enlarged Board of Appeal in G2/21, post-filed data will not rescue the applicant where such support is absent from the application as filed.

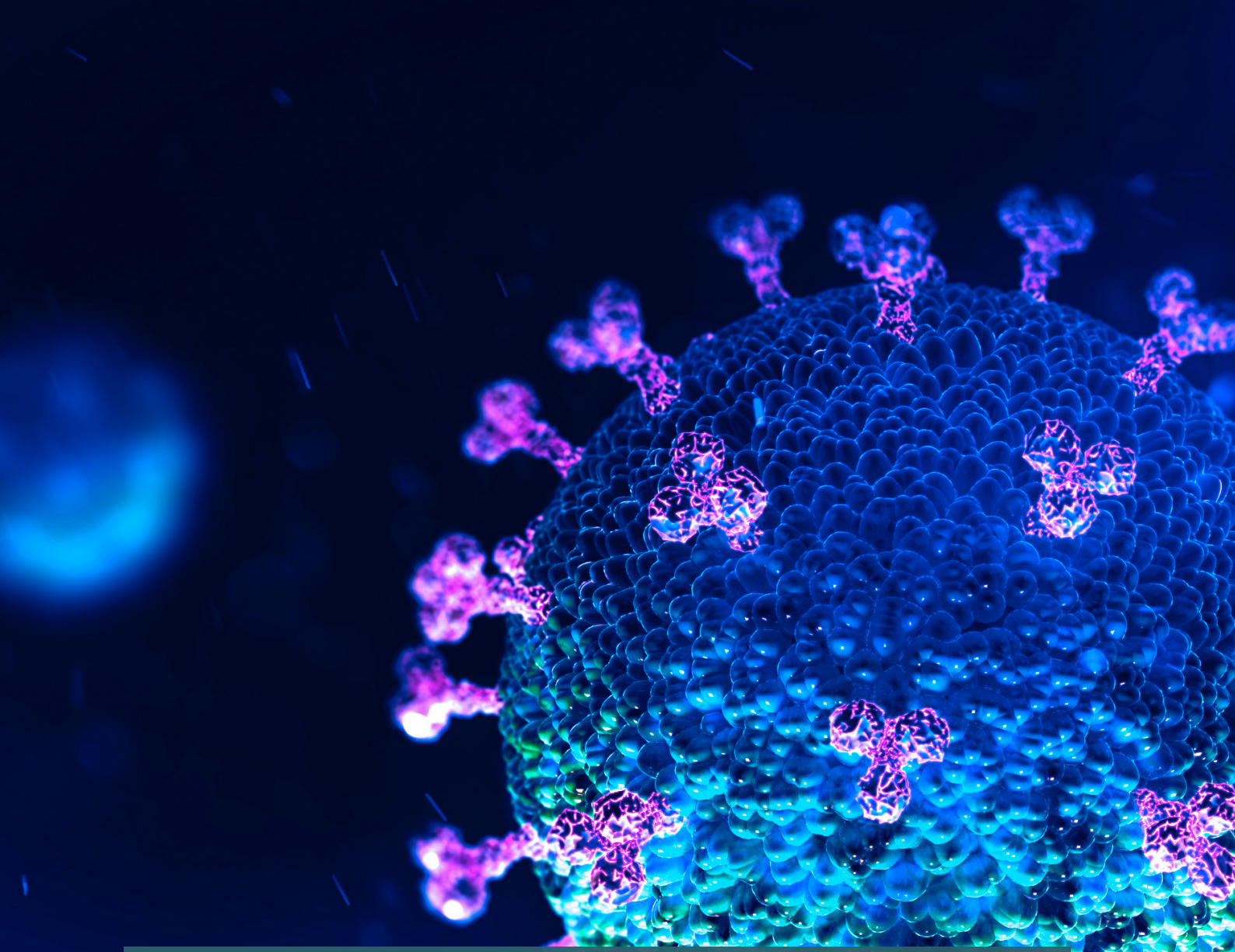
In EPO opposition the burden of proof initially resides with the opponent to substantiate the facts it alleges. For insufficiency, the EPO sets a high standard of establishing "serious doubts, substantiated by verifiable facts" that the skilled person would not be able to work the invention as claimed, across the whole scope. An understanding of antibody case law also is key, particularly when it comes to both attacking and defending from a sufficiency challenge.

For example, in T1345/20 (Diagnosis of Gaucher's disease/26-09-2023), the BoA noted that the patent contained no experimental evidence and/or information on how to obtain the claimed antibody and the target was particularly challenging. It was therefore enough for the appellant to establish a lack of sufficiency of disclosure by merely raising serious doubts, e.g. by comprehensive and plausible arguments that the common general knowledge and the patent provide insufficient information to reliably obtain the claimed antibody.

On the other hand, in T1394/21 (VISTA and PD-L1-antagonists/25-04-2023), the patent claimed an anti-VISTA antibody for use in treating cancer but the patent did not sufficiently disclose the antibody 13F3 which was the only antibody disclosed in the patent. The BoA found the patent did not contravene A83. They concluded that with the teaching provided in the application as filed, and the CGK available at the time, the skilled person would be able to perform routine experimentation and provide the requisite antagonistic anti-VISTA Ab.[7]

[6] E.g. T 3165/19 and T885/21.

[7] A similar approach was taken by the BoA in T0835/21.



Conclusion

Overall, there are a lot of similarities between the outcomes of oppositions and appeals between antibody-related cases and reference cases.

Surprisingly, for both antibody-related and reference cases, opposition seems to favour opponents, with the vast majority of oppositions having a final outcome of either revocation or amendment. Moreover, and perhaps even more surprisingly, appeals following rejected oppositions also appear to favour the opponent. With over 66% of appeals following opposition rejection ending in revocation or amendment of the patent. Following a rejected opposition, a much greater percentage of appeals ended in revocation of the patent in antibody related cases compared to reference cases.

From the above data, it is apparent that EPO opposition is an effective forum for 3rd parties to attempt to mitigate potential freedom-to-operate risks. With costs being relatively low and with the ability to file anonymously, filing EPO oppositions should form an integral part of a company's strategic planning when developing an antibody product and taking it through the various stages to market. Similarly, patent owners should carefully consider amendments made during prosecution and should mount a robust defence in the event that their patent is opposed.

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