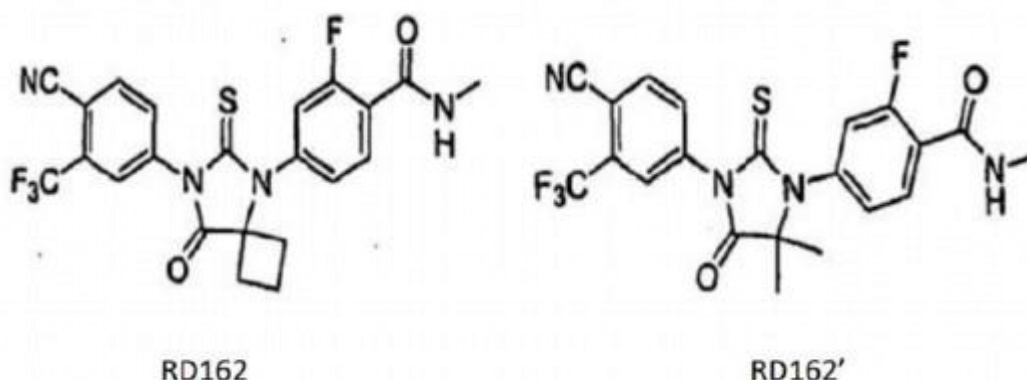


Accord Healthcare Ltd v Regents of the University of California [2024] EWHC 2524 (Pat)

On 8 October 2024, Mr Justice Mellor handed down his judgment in *Accord Healthcare Ltd & Others (hereafter “the Claimants”) v (1) Regents of the University of California and (2) Astellas Pharm Europe Ltd (together “Astellas”)* [2024] EWHC 2524 (Pat), finding that EP (UK) 1 893 196 B2 (the “Patent”) and SPC/GB13/079 was not obvious. The Claimants’ arguments on sufficiency which were run as a squeeze also failed.

The Patent claimed the compound enzalutamide for the treatment of hormone refractory prostate cancer (“HRPC”), marketed under the brand name Xtandi, with a priority date of 29 March 2006. Enzalutamide is an anti-androgen hormone therapy that blocks androgen receptors (“AR”).

The Claimants relied on two pieces of prior art independently, both of which originated from the inventors discussing their work; a series of slides presented as part of a lecture (the “Slides”); and a poster depicting a step-wise development of molecules based on structure-activity relationship (“SAR”) studies (the “Poster”). The Slides and the Poster were made available to the public at a conference in September/October 2005 and both disclosed what was agreed to be the closest prior art molecule, referred to as RD162. The structure of RD162 differed from that of the claimed compound RD162’ (enzalutamide) by virtue of a different substituent at the bottom right of the central thiazolidinone ring (“Position X”). RD162 had a cyclobutyl group, whereas RD162’ had a dimethyl substituent as shown below.



Obviousness over the Poster

The Claimants sought to argue that it would have been ‘*immediately obvious*’ from the Poster to develop RD162’, and that, in the alternative, it would have been ‘*obvious to do a SAR*’ that would have led the Skilled Team to RD162’. The Skilled Team in this case comprised a cancer biologist and a medicinal chemist.

1. ‘*Immediately obvious*’

Mellor J outlined a number of issues with the Claimants’ expert evidence on whether it would have been immediately obvious to the Skilled Team to develop RD162’ starting from the Poster. One issue was that the Claimants did not explain why the Skilled Team would start by considering making a change from the cyclobutyl group at Position X. Instead, the evidence was put forward on the assumption that the Skilled Team would begin the development on the above assumption that there ought to be a change at Position X. The Judge observed that a case run on obvious immateriality does not absolve the Claimants from having to consider the actual teaching of the prior art or allow them to generalise it into oblivion. He also noted that there is no separate body of law that is applicable if the change from the prior art to the claim is said to be ‘*immaterial*’ or ‘*trivial*’. There is only the statutory question, “*is it obvious?*” He also observed that, in general terms, issues of ‘*immateriality*’ or ‘*triviality*’ are not well suited to the field of medicinal chemistry, although this will depend on the context. Mellor J therefore rejected the Claimants’ argument finding the ‘*immediately obvious*’ case to be driven by hindsight.

2. 'Obvious to do a SAR'

The Claimants' supplementary case was one said to have been developed through the cross examination of Astellas' medicinal chemistry expert. The Claimants sought to establish that it would have been obvious to do a SAR study, starting from RD162, to develop their own molecule. Although this was agreed, what would occur following the SAR was disputed. The Claimants attempted to put forward a number of arguments as to why, having done a SAR, the Skilled Team would have arrived at RD162', including being instructed to do so by a department responsible for patent applications to make a 'back-up' compound. As above, Mellor J dismissed these arguments as being driven by hindsight. Although the Skilled Team would do a SAR using ED162 as their starting point having read the Poster, they would have been motivated to develop a novel compound which would have taken them further away from RD162 than the change of substituent at Position X.

It is interesting to note that Mellor J expressed that it would be possible to envisage a finding of obviousness in this case, had it been established in the written evidence in chief that RD162' would have been a byproduct of a SAR study and subsequent testing of RD162. Instead, the 'obvious to do a SAR' case was developed in cross examination, with knowledge of RD162' as the target molecule, thus driven by hindsight.

Obviousness over the Slides

Mellor J similarly held that claim 1 was not obvious over the Slides, although he noted that the arguments here were more finely balanced (he admitted that he had changed his mind on obviousness over the Slides more than once). However ultimately, as with the obviousness arguments concerning the Poster, the Claimants failed to explain why the Skilled Team would initially consider making the change to RD162 at Position X in order to arrive at R162'.

The Slides contained a pharmacophore, which is an overview of the author's views of different interactions of the molecule within the AR binding site, with three targets being marked for investigation. One of these targets contemplated a dimethyl substituent at Position X. The Claimants argued that had the authors intended to communicate that this was not to be further investigated they would have presented the pharmacophore in a different way. Astellas said that the Slides were considering ways to improve the agonist, and the reader could see a deliberate decision to change the dimethyl substituent. It would therefore not have been obvious to revert back to a dimethyl without reason to do so. Mellor J ultimately agreed that the Skilled Team would have considered it a backwards step to change from cyclobutyl to dimethyl.

Mellor J also outlined three overarching principles that it is useful to bear in mind when assessing obviousness. First, if steps are obvious it should be possible to explain this clearly and in the evidence in chief. Second, in litigation there is considerable focus on the route(s) to obviousness and obstacles. Finally, it is unsurprising that with skilful cross-examination, where the focus is on the target, the obviousness arguments appear to have force. Although it is possible for an obviousness argument to be proved through cross examination, there must also be sufficient primary evidence on the point.

This case therefore raises key points for practitioners about the preparation of expert evidence when trying to invalidate a patent for obviousness. The evidence in chief should set out clearly what steps the skilled person would take starting from the teachings of the prior art. If the claims in the patent are obvious, then these steps would lead the skilled person to the invention. Only relying on cross examination with knowledge of the target without a positive explanation as to why seemingly small changes to the prior art would have been implemented will not satisfy the legal test of '*is it obvious?*'

The judgment also addressed issues of secondary evidence, although Mellor J ultimately did not place any weight on these issues.

Validity – Sufficiency/Plausibility

The Court also rejected the sufficiency attack on the Patent, holding that it disclosed a novel molecule RD162', that it was plausible that RD162' would work (and does in fact work) and that the Patent plainly made a technical contribution.