Probing the bounds of patent law

Advanced Cell Diagnostics v Molecular Instruments [2024] EWHC 898 (Pat)

On 23 April 2024, Mr Justice Meade handed down his judgment in the dispute between Advanced Cell Diagnostics (ACD) and Molecular Instruments (MI).

ACD is the proprietor of two European patents which concern the *in situ* detection of nucleic acids. EP (UK) 1 910 572 ("**EP 572**") and EP (UK) 2 500 439 B1 ("**EP 439**") (referred to collectively as "the **Patents**") have largely identical specifications but the claims of EP 572 are process claims whereas the claims of EP 439 are to kits and products for nucleic acid detection. MI, a US-based company, manufactures and sells products in the US which are imported into the UK by its customers. ACD alleged infringement of both patents by MI as a joint tortfeasor along with its UK customers and MI counterclaimed for the Patents' revocation.

Briefly on the technology, hybridisation assays are used to detect particular strands of nucleic acids within a given sample using nucleotide probes (nucleic acid fragments). The probes (or 'capture probes') are designed to be complementary to the target of interest, and if the target is present will hybridise it (i.e. bind to it) to form a stable duplex. Label probes can be used which bind to the capture probes and produce a signal, indicating the presence of the target nucleic acids. Using multiple capture probes results in the attachment of more signal-detecting particles resulting in higher detection sensitivity. Whilst *in vitro* hybridisation methods are applied to nucleic acids which have been extracted from their source, *in situ* hybridisation (ISH) assays provide information whilst preserving the integrity of the cell.

Claim construction – what does 'overlapping' mean?

The Patents disclose a method (EP 752) and a kit (EP 439) for detecting nucleic acids using ISH assays. The claims require *inter alia* a label probe, and two or more capture probes, for each nucleic acid target. The capture probes must comprise a section which is complementary to a non-overlapping section on the nucleic acid target, and a section which is complementary to a non-overlapping section on the label probe (as depicted in Figure 3). This is to ensure the probes do not compete for binding with the same nucleic acid targets, which could weaken the connection and cause instability.

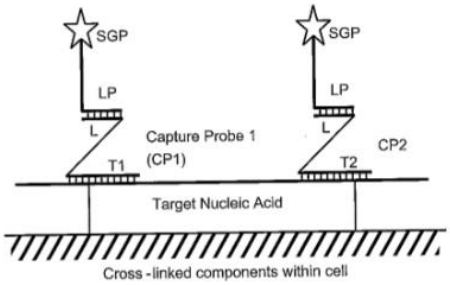

Fig. 3

MI's non-infringement case centred on the fact that in its system the sections overlap, which increases the system's specificity. ACD disputed any advantage conferred by the overlap, and argued that in any event MI's system still has the benefit of using two probes rather than one and therefore infringed. A critical issue for the judge turned on the construction of 'non-overlapping'.

Drawing a parallel with the Court's decision in *Catnic* (in which a claim to 'vertical' encompassed a small degree of variation as long as the weight-bearing function of the product was not impeded), Meade J found that 'non-overlapping' should not be read so strictly as to mean 'completely non-overlapping'. The question was simply whether the two probes could each form stable duplexes such that there was a benefit associated with using two probes rather than one. The Judge preferred ACD's evidence and held that on a normal construction, MI's system infringed.

Infringement under the doctrine of equivalence

Meade J also considered infringement by equivalence, applying the test from *Actavis v Lilly*[1]. Taking as the 'inventive core' the better specificity achieved by the use of two probes, in answering to the first question Meade J considered the variant to achieve substantially the same result (good specificity) in substantially the same way (via two stable duplexes). It followed that, in the knowledge that the variant worked, it must be obvious to the skilled person *how* it worked (question 2). In answering the third question, Meade J found there is nothing in the Patents which requires strict compliance with the literal meaning of the claims. He therefore also found infringement by equivalence.

Was MI a joint tortfeasor with its UK customers?

Regarding joint liability, a distinction was drawn between customers to which MI provided only general and standard directions by way of protocols, and other customers to which MI provided specific troubleshooting, tips and tailored advice. Applying the principles set out by the Supreme Court in *Fish & Fish v Sea Shepherd UK*[2], Meade J found the former went no further than "mere facilitation", whereas the latter amounted to assisting customers pursuant to a common design by working a method which would have infringed EP 572.

Anticipation and obviousness

Turning next to validity, MI's main attack was based on anticipation and/or lack of inventive step over a prior art citation "Collins", either alone, or read together with the prior art "Kern", a citation referred to in Collins. As readers will know, a very high threshold applies for combining prior art documents for the purposes of anticipation. On these facts the cross-reference to Kern was too general, and the anticipation attack failed (neither document alone contained a clear and unambiguous disclosure). Meade J clarified that whilst there is no absolute rule against combining documents for the purposes of anticipation in UK proceedings, it is a requirement that one document points to the other with "clear and unmistakable directions".

On the issue of obviousness, the key dispute centred on whether the skilled person would think there were reasonable prospects of successfully using the hybridisation assay disclosed in Collins in an *in situ* setting (as claimed). Linked to this, was a dispute between the parties as to the "mindset" of the skilled person. ACD submitted that whilst there was no *actual* problem in doing so, there was a perception at the time that taking an *in vitro* technique *in situ* would have little or no expectation of success , and that this was relevant in assessing obviousness. Meade J was not persuaded that this "mindset" formed part of the CGK, not least because there existed techniques which had done the same thing and been successful; it was merely an empirical task which might pose some practical difficulty, but which the skilled person would expect to overcome in due course. In the absence of specific reasoning as to why the skilled person would *not* have an expectation of success, the claims were held to be

[1] *Actavis UK Limited and others v Eli Lilly and Company* [2017] UKSC 48.
[2] *Fish & Fish v Sea Shepherd UK* [2015] UKSC 10.

obvious. This conclusion was not hindered by the availability of other routes the skilled person could have taken based on the prior art.

Insufficiency

As the case was decided on obviousness, Meade J only made a few remarks on MI's insufficiency attacks, which were advanced as squeezes.

The first linked to whether there was an expectation of success (as discussed above) of moving from *in vitro* to *in situ*; if ACD maintained that transferring an *in vitro* assay into an *in situ* format would not be obvious to the skilled person due to low/no expectation of success, Meade J found the patents would be insufficient as they do not contain any data to demonstrate that the claimed method or kits work *in situ*. The second argument concerned breadth of claim insufficiency; if a successful ISH assay requires a careful balancing of different parameters as ACD contended, it is not plausible that the invention will work across the scope of the claims. Meade J disagreed; the invention did not require this and therefore the claims were not about "relevant ranges" in the *Illumina*[3] sense.

Ultimately, the Patents were found to be invalid for obviousness, but had they been valid MI would have infringed the process claims in EP 572 but not the claims in EP 439 to kits and products.

Whilst the decision turned on its facts, the judgment is strewn with various points of interest relating to claim construction, the influence of 'mindset' on the CGK and the mosaicking of documents. It also highlights the difficulty of relying upon 'no expectation of success' as a defence to obviousness in the absence of specific evidence.

[3] *Illumina v Latvia MGI* [2021] EWHC 57 (Pat).