Illumina vs MGI: the High Court Considers Sufficiency, the Doctrine of Equivalents and Obviousness

The High Court of England and Wales has recently handed down its judgment in Illumina Cambridge Limited vs Latvia MGI Tech SIA and others. This is one of the last judgments handed down in the High Court by Mr Justice Birss, who was recently elevated to the Court of Appeal. The judgment touches on a number of important aspects of patent infringement and validity, including the first application of the recent Supreme Court decision in Regeneron Pharmaceuticals Inc vs Kymab Ltd relating to sufficiency.

In this briefing we consider four aspects of the judgment: one relating to sufficiency of disclosure, one relating to infringement under the doctrine of equivalents, and two relating to obviousness.

Background to the case

The technology at issue concerned reagents and processes to carry out "sequencing by synthesis", a method of using four different fluorescently labelled nucleotides to sequence DNA. Despite the technology relating to DNA sequencing methods, many of the explanations provided in the judgment are of course of relevance to other technical fields.

The DNA sequencing method at issue involves successive reaction cycles comprising the steps of (i) adding a capped, labelled nucleotide to a growing DNA chain, (ii) reading the (fluorescent) signal from the label to determine which one of the four possible different nucleotides has been added, and (iii) cleaving the cap and the label to expose a reactive site for a further 'add-read-cleave' cycle.

In total, five Illumina patents (the '578, '289, '433, '412 and '415 patents) were at issue and four systems marketed by MGI (known as Standard MPS, Cool MPS, the 'two colour variant', and DNBSEQ E) were alleged to infringe various of the Illumina claims.

The judge concluded that four of the patents (as amended during the proceedings) were found to be both valid and infringed, with the '412 patent found to be invalid for lack of inventive step.

A patent can only be insufficient in the "Regeneron" sense if a "relevant" range is non-enabled across its whole scope

In *Regeneron*, the Supreme Court ruled that a claim which seeks to protect products that cannot be made by the skilled person at the effective filing date using the disclosure in the patent will be insufficient, subject to *de minimis* or wholly irrelevant exceptions. In this regard, the Supreme Court made a distinction between "relevant" ranges in a claim, which are denominated by reference to a variable which *"significantly affects the value or utility of the product in achieving the purpose for which it is to be made"*, and ranges that are not "relevant", which are denominated by *"some wholly irrelevant factor"*. The requirement to show enablement across the whole scope of the claim was judged to apply only across a "relevant" range. The present judgment expands upon and applies this general principle.

MGI argued based on *Regeneron* that the sequencing by synthesis process claims in the '578 and '433 were insufficient, on the following grounds:

> (a) The claimed sequencing methods include *"at least one incorporation"* of a capped fluorescent nucleotide. Thus the claims are open ended with respect to the number of 'add-read-cleave' cycles, but the data in the patent only present results for a limited number of cycles, and so performing the method over a larger number of cycles is not enabled (the "read lengths" issue); and
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> (b) The claimed methods cover use of nucleotides, linkers and labels which would not work in practice, such as nucleotides which could not be incorporated, or linkers which could not be cleaved under conditions which do not damage the DNA (the "impractical linkers" issue).

The judge started out by confirming that whilst the case before the Supreme Court in *Regeneron* related to product claims, the same principles also apply to process claims, as in the present case.

The judge then considered the concept of a "relevant range", and emphasised that it is important to distinguish between ranges that are relevant in a *Regeneron* sense and ranges that are not. For ranges relevant in the *Regeneron* sense to be sufficient, there must be enablement across the whole scope of the claim within that relevant range (subject to *de minimis* exceptions) at the effective filing date. This means that a skilled person must be able to work the invention across the whole relevant range at that date without undue burden. If an embodiment within a relevant range in the *Regeneron* sense is not enabled at that date then the fact it could be made at a later date as a result of further technical advances, will not save the claim from insufficiency. That is the case even if the later embodiment could never have been made without the teaching of the invention disclosed in the patent.

An example of a range that is not relevant in the *Regeneron* sense is a descriptive feature in a claim (whether structural or functional) which can cover a variety of things, but for which that variety does not significantly affect the value or utility of the claimed product or process in achieving its relevant purpose. The relevant purpose is judged in all the circumstances, starting from

the terms of the claim itself but also, where appropriate, by reference to the "essence" or "core" of the invention (a concept favoured by UK judges). For a range that is not relevant in the *Regeneron* sense, the skilled person must still be able to make a suitable selection, without undue burden, in order for the claim to be sufficiently disclosed. However provided that is so at the effective filing date, such a feature will not be insufficient simply because it embraces embodiments which had not been invented at that date.

By way of example, the judge referred to a new type of teapot that was inventive and useful because its spout was shaped in a new way so as not to drip. A claim might be drawn to a teapot with the spout shaped in that special way. This claim would cover teapots made of different materials, including materials that had not been invented yet. The fact that teapots made of such novel materials could not be made at the effective filing date does not make the claim insufficient, because the "essence" of the invention lies in the spout shape, not the teapot's material. The material is accordingly not a relevant range in the *Regeneron* sense. Thus, the correct test for sufficiency is to ascertain whether a skilled person could select, without undue burden, a suitable material from which to make the teapot at the effective filing date. That is clearly the case (e.g. the skilled person would know china is suitable, but chocolate is not) and so the claim is sufficient.

One important take-home message from this analysis is that the judge identified what the skilled person is able to do without "undue burden" as the correct test to apply both when assessing (a) whether a claim is enabled across a full range that is relevant in the *Regeneron* sense and (b) whether the skilled person can make a suitable selection from within a range that is not relevant in the *Regeneron* sense.

Returning to the facts of the present case, the judge ruled that the "essence" of the invention is a sequencing method whose utility derives from the use of a capped, labelled nucleotide in order to determine the identity of that nucleotide. The claims were relatively narrowly defined at the point of the invention, in that the capping group was specified to be azido methyl. Neither the individual type of the other components employed (nucleotide, linker, label etc.) nor the number of read cycles significantly affect the utility of this method. Thus, neither the "read length" nor "impractical linkers" issues were found to be relevant ranges in the *Regeneron* sense. It was found that the skilled person could select suitable components for use in the method without undue burden, and thus the claims were deemed sufficient.

This decision provides a helpful summary and application of the principles laid down by the Supreme Court in *Regeneron*, and draws a distinction between ranges that are "relevant" in the *Regeneron* sense and those which are not. In particular, Justice Birss's comment [at para. 278] that *"once the concept of a relevant range is properly understood, I think it will be an unusual case in which the kind of ordinary descriptive or functional language one sees in most patent claims will be regarded a relevant range in the Regeneron sense"* is likely to provide comfort to patentees that the *Regeneron* decision has not in fact created a significantly higher sufficiency standard for them in the UK or moved the UK further out of line with the EPO, where most of their patents will be granted.

A narrow definition of a term in the description can preclude the successful application of the doctrine of equivalents

In a landmark 2017 decision, the Supreme Court in Actavis UK Ltd and others vs Eli Lilly & Co. introduced a doctrine of equivalents to patent infringement in the UK. To assess whether a variant of a claimed invention that does not infringe on normal interpretation of the claims is nevertheless an infringing equivalent, a three-step test must be applied:

> (i) notwithstanding that it was not within the literal, or normal, meaning of the relevant claim(s) of the patent, does the variant achieve substantially the same result in substantially the same way as the invention;
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> (ii) would it be obvious to the person skilled in the art, reading the patent at the priority date, but knowing that the variant achieves substantially the same result as the invention, that it did so in substantially the same way as the invention; and
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> (iii) would such a reader of the patent have concluded that the patentee nonetheless intended that strict compliance with the literal meaning of the relevant claim(s) of the patent was an essential requirement of the invention.

In order to establish infringement by way of equivalence, the answers to these questions must be "yes", "yes" and "no".

In the present case, the judge had to consider whether MGI's Cool MPS system infringed the method claims of the '578 and '412 patents. The claims at issue involved a step of *"incorporation"* of a nucleotide to a growing DNA chain wherein a part of that nucleotide *"is linked to a detectable label"*. It was common ground between the parties that in the Cool MPS system, such a nucleotide was not incorporated into the growing DNA strand in a single step. Rather, the incorporation happened over two steps: first, a nucleotide without a detectable label was added to the DNA stand; and second, an antibody linked to a fluorescent label was added which became associated with that nucleotide. The infringement issue therefore primarily turned on whether the term *"incorporation"* embraced the two-step process, or whether it was limited to a single-step reaction.

On a normal interpretation of the claims, the judge considered the definitions of *"incorporation"* provided in the descriptions of the '578 and '412 patents to be determinative.

In the '578 patent, *"incorporation"* had been broadly defined, meaning that the nucleotide *"becom[es] part of"* the relevant (e.g.) DNA molecule. This led to a finding that the relevant claim of the '578 patent embraces the two-step process of the Cool MPS process, which thus infringes on a normal interpretation.

In the '412 patent, however, a different definition of *"incorporation"* was provided, that was limited to a specific chemical reaction for attaching the (labelled) nucleotide to the growing DNA chain. Consequently the judge construed the relevant claim more narrowly in light of this definition, such that the claim excluded the two-step process. Cool MPS thus was found not to infringe the '412 patent on a normal interpretation.

Turning to an assessment of equivalents, the parties did not dispute that the answers to the first two *Actavis* questions were "yes" and "yes". All therefore turned on the third *Actavis* question, where the judge again found the definitions of the term

"incorporation" provided in the patents to be determinative.

The judge considered equivalents for the '578 patent as a precaution, in case his finding of infringement on a normal interpretation of the claims were to be incorrect. In particular, if the term *"incorporated"* should be limited to a single-step process on a normal interpretation, then the judge was of the view that the patentee could not have intended strict compliance with such a construction given the broad definition of *"incorporated"* provided in the description. The answer to the third *Actavis* question is therefore "no" and Cool MPS would still infringe the '578 patent, as an equivalent. Given the outcome of other judgments relating to the doctrine of equivalents following *Actavis*, this finding is likely to be unsurprising to most observers.

Perhaps more surprisingly, however, in the case of the '412 patent it was found that the reader of the patent ***would*** have considered the patentee to intend strict compliance with the literal interpretation of the claim, because of the narrow definition of *"incorporation"* provided in the description. In this regard, the judge emphasised that it does not matter ***why*** the patentee chose to define the term narrowly in the description; rather, what matters is that the patentee, as a matter of fact, went out of its way to define that term in a *"clear and simple"* way. The third *Actavis* question was thus answered "yes" and Cool MPS was found not to infringe the patent as an equivalent. This conclusion was reached despite the fact that, as the judge admits, the Cool MPS system was an immaterial variant to the invention claimed in the '412 patent.

This decision therefore provides some guidance on how to assess the third *Actavis* question. In particular, it serves as a warning to patentees that if infringement is found not to have occurred on a normal interpretation of the claim due to a restrictive definition of a term presented in the description, it may be difficult to rescue the situation by invoking the doctrine of equivalents. The outcome is perhaps in line with what might have been expected pre-*Actavis*, where the definition of *"incorporation"* in the description of the '578 and '412 patents would likely have been important in the pre-*Actavis* "purposive" construction of the claim.

One further potential point of interest is that it is unclear how much turned in this case on the judge's characterisation of the definition of *"incorporation"* in the '412 patent as being *"clear and simple"*. Whether a patentee would have more success invoking equivalents in the case of a definition that is not *"clear and simple"* (e.g. is unclear, vague and/or complex), which the courts would nonetheless have to construe in a particular way when assessing infringement under a normal interpretation of a claim, remains to be seen.

The skilled person for determining obviousness does not have to be the notional addressee of the patent

During assessment of the validity of the '578, '289 and '433 patents, one issue that arose was in the correct definition of the skilled person. The skilled person for assessing obviousness is often the same as the skilled person for the purposes of assessing sufficient disclosure (i.e. the notional addressee of the patent). However, that need not necessarily be the case.

A patentee is allowed to direct the patent to whoever they see fit. In some cases, the invention may lie in combining ideas from disparate technical fields. The notional addressee of the patent in such cases may be a team with expertise in each of those fields. However, it would be unjust for this team to be the relevant skilled person for assessing inventive step, because in assembling this team the art is defined in an overly narrow way (with consequences on, e.g., what that skilled team would consider to be "common general knowledge"). Another example of where it might not be appropriate for the skilled person for determining obviousness to be the notional addressee is in cases where the invention lies in identification of the problem itself.

The judge reviewed the case law on this matter and devised a test to identify the skilled person for assessing obviousness in instances when that person is different from the skilled person for assessing insufficiency. The test involves the following steps:

(i) start by asking what problem the invention aims to solve;

(ii) that leads one in turn to consider what the established field which existed was, in which the problem in fact can be located; and

(iii) it is the notional person or team in that established field which is the relevant person or team making up the person skilled in the art.

The skilled person for assessing obviousness must therefore be in an "established field". The breadth of that field will depend on the facts and what was going on in reality at the priority date. The selection of this field applies hindsight – it is not necessary for the people in the relevant field at the time to have perceived the particular problem solved by the invention, or perceived the problem in the manner it is now characterised.

The correct application of this test is likely to be heavily dependent on the facts of a given case, and *evidence* of what was going on in reality at the priority date may prove decisive. The judge concluded in the present case that "sequencing by synthesis" was, on the facts, a sufficiently well-established field for the skilled person to be narrowly defined as a team working on research into sequencing by synthesis. Thus, having applied the newly developed test, the judge concluded that in this case the skilled person for assessing obviousness *was* the same as the skilled person for assessing insufficiency. Nonetheless, he went on to find that, on the facts, the claims of the '578, '289 and '433 patents were non-obvious to that skilled person.

Single chemical species are not necessarily obvious even if each of their component parts are individually obvious and there is no synergistic effect

The relevant claim of the '415 patent was directed to a nucleotide labelled with a specific dye-linker conjugate. It was not disputed that this claim was infringed on its normal interpretation by the Standard MPS system. MGI argued that such a molecule lacked an inventive step as it was a mere collocation of components known in the prior art: the specific dye was known to be a dye suitable for making labelled conjugates for use in biological systems, the specific linker was also known to be useful in combination with nucleotides, and each of the dye, linker and nucleotide act independently (there is no synergistic effect). This argument relied on precedent set by Sabaf SpA vs MFI Furniture Centres Limited and others, in which the invention was a mechanical one.

The judge agreed with MGI to the extent that individually, use of the particular dye and use of the particular linker were obvious

choices for incorporation into a dye-linker-nucleotide complex. Further there was no evidence of a synergistic effect between the components. However, the judge ruled that in the case of a single chemical molecule, there is always some risk that, when combining two known elements into a single conjugate (here, the dye and the linker-nucleotide conjugate), the two will interact adversely. For example, interactions between the components could prevent the dye from fluorescing.

Unlike in *Sabaf*, there is nothing inherent in either of the elements to mean that each element is incapable of interacting with the other element. The skilled person will not know whether such an interaction arises until the combined molecule is synthesised and tested. The test may not be burdensome, but that does not matter; the fact is a test is required as the different elements in a conjugate are not *a priori* immune from the effects of the other(s).

It is important to note that this is a decision on the facts by a first instance court that does not *prima facie* change the UK stance on obviousness. However, in light of this decision, it does seem less likely than before that an obviousness attack on conjugate chemical or biological molecules based on mere collocation of prior art will succeed before the UK courts.

Conclusions

In summary, *Illumina* provides some important guidance for patentees, defendants and patent practitioners on the issues of sufficiency and infringement by equivalents, and also contains some interesting points on obviousness determination.

This may not be the final word on these matters if the judgment is appealed by MGI. However, with the elevation of Mr Justice Birss to the Court of Appeal, it seems likely that the thinking behind *Illumina* will be reflected in other, higher-level judgments in the future.

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