Regeneron Pharmaceuticals Inc

v

Kymab Ltd

UK Supreme Court ruling

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Executive Summary

The UK Supreme Court has overturned a decision from the Court of Appeal to find two of Regeneron's transgenic mouse EP/UK patents invalid because they were insufficient.

This judgement has returned the bar on sufficiency requiring support for practically every embodiment.

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Background

Patents in question were in the name of Regeneron Pharmaceuticals Inc (Regeneron): **EP/UK1360287** (see **here**); and **EP/UK2264163** (see **here**).

The two patents described and claimed transgenic mice capable of producing humanised antibodies.

Regeneron alleged infringement by Kymab Ltd (Kymab).

Kymab counterclaimed invalidity, on the grounds of among others, lack of sufficiency.

At the High Court, the patents were held infringed but invalid.

The Court of Appeal overturned the decision on validity finding that the patents were valid and infringed.

Kymab appealed to the Supreme Court.

State of the Art

At the relevant date, it was known that antibodies (Ab) could be used to treat disease in human hosts and mice were identified as suitable commercial production platforms.

There were two problems linked with this:

i) rejection of mouse Abs by the host; and

ii) an impaired Ab response in mice transplanted with human Ab genes.

Abs are produced by B-cells and in mice and humans they carry both, light & heavy chains.

Gene segments for variable regions of Abs comprise variable (V) and joining (J) segments in the light chain locus, and variable (V), diversity (D), and joining (J) segments in the heavy chain locus.

Natural recombination of somatic genes leads to a huge variety of antibodies being produced with different amino acid sequences in the antigen-binding regions, providing a corresponding repertoire of Abs.

Inventive concept

The solution to the problems associated with production of Abs in mice was to create a hybrid (chimeric) Ab gene structure, called a “Reverse Chimeric Locus” comprising the murine constant region and the human variable region.

The gene structures are stably integrated into the mouse genome for the production of hybrid antibodies, and mouse constant regions were removed from isolated B-cells prior to mass production.

This enables the production of human Abs that respond naturally to Ag challenge and therefore mimic natural immune system.

On encountering Ags, B-cells proliferate and differentiate, enabling the production of a diverse spectrum of Abs against an Ag derived single target peptide.

Sufficiency

In accordance with both UK IP law and the EPC, a set of claims to a single product or a range of products is required to be “enabled”, which means that the skilled person must be able to put the invention into effect, with no more than common general knowledge at the priority date, and without “undue experimental burden”.

This is termed the sufficiency requirement of a patent and ensures that the extent of the monopoly granted corresponds to (and does not exceed) the contribution to the art.

Earlier rulings

The High Court (Judge Henry Carr) found infringement because Kymab used transgenic mice, but held the claims invalid for lack of sufficiency.

The Court held that the example for producing the claimed mouse would not have worked because the method to insert and delete large sections of DNA was not known.

The Court of Appeal took a different view in 2018 and found the claims both valid and infringed.

Lord Justice Kitchin agreed that the example of the patent would not have worked, but that common general knowledge could be used to make **obvious changes**.

Importantly he reasoned that this would enable the skilled person to make one type of transgenic mouse within the scope of the claims, and that this was sufficient, despite the skilled person being unable to make **all** types of mice within the claimed scope and in the light of the common general knowledge.

Supreme Court judgement

The “disclosure in the patent should enable substantially all products within the scope of a product claim to be made by the skilled person at the priority date”.

The extent to which the human Ab variable region could be incorporated was understood to be a crucial factor in determining the repertoire of antibodies that could be produced.

The claims conferred a monopoly over mice incorporating any or all of the human variable region when a hybrid gene structure comprising the whole variable region was achieved only with further inventive processes.

Lord Briggs - an invention cannot be considered enabled if it does not permit the skilled person to make it. The invention was held not enabled over “substantially the whole range of products” claimed.

Kymab’s appeal was upheld, and the patents held to be invalid for lack of sufficiency.

The case marks a return to a more traditional approach to sufficiency with far reaching implications.