The Scope and Infringement of Patents Claiming Strains of Bacteria

Understanding the scope of a patent claim is of utmost importance when assessing the strength and value of a portfolio and making appropriate commercial decisions, and when drafting new applications or overcoming objections in examination.

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Of the patents granted by the European Patent Office in 2019 and 2020 claiming naturally-occurring bacteria, 45% are limited to specific deposited strains[1]. These claims recite, for example: "*A composition comprising the strain of Bifidobacterium breve deposited under accession number X*", often with medical use claims and method claims limited to the specific deposited strains. Despite the large number of such claims that are being granted and have been granted for a number of years, it is not well-established exactly what scope these claims have, what protection they provide, and how might they be infringed.

Live bacteria represent extremely complex products and are far more complex than antibody therapeutics, for example. Also, whilst patent practice and case law relating to antibody patents is well-established and settled, the immaturity and rapid development of the microbiome field means that there have been very few disputes regarding patents claiming bacteria to provide guiding case law and to help establish patent examination practice.

Furthermore, there is no scientific consensus regarding what a bacterial strain is. Indeed, Van Rossum *et al*. comment that "*a widely accepted, biologically meaningful definition of strain remains elusive*"[2]. In this context, it is hard for patent practitioners to be certain of the scope of a claim that refers to a deposited bacterial strain.

Patent claims directed to bacterial strains almost always refer to a deposit in a culture collection and Van Rossum *et al*. suggest that, in relation to culture collections, the term "*strain*" is understood to refer to "*descendants of a single isolation*". If such an interpretation was to be followed, this could mean that claims limited to a deposited strain are extremely narrow and infringed only by a bacteria that is derived from the same deposit. Even then, after a few generations and mutations, there may be detectable differences between the deposited strain and the potentially infringing strain. However, analysis of relevant judgments from various jurisdictions suggests that claims limited to specific strains are likely to have useful scope, if the patent includes key information, as discussed below.

One of the only cases to consider the scope of a patent claim limited to a deposit was *Shanghai Finc v. Tianjin Lvshengpengyuan and Hongbinhesheng* at the Beijing IP Court[3]. The patent at issue claimed a deposit for a mushroom, rather than a bacteria, but the process that the court followed is still relevant and provides useful guidance on how another court might consider similar issues. Shanghai Finc held a patent with a claim directed to a specific mushroom deposit and it accused the defendants of infringing the claim by selling their mushrooms. The defendants argued that their mushrooms were not of the same strain, and so the court had to consider the scope of the claim, and how it should be determined whether the allegedly infringing mushrooms fell within its scope.

In order to answer these questions, the court carried out a comprehensive analysis, looking first at morphological characteristics and then sequencing data. The sequencing analysis is particularly interesting because the defendants argued that the court should use whole genome sequencing, which revealed differences between the deposited strain and the infringing strain. However, the court dismissed this approach on the grounds that it could find no consensus in the field regarding what threshold of similarity defined the limits of a mushroom strain, as discussed above for bacteria. Instead, the Beijing IP Court decided to use a particular marker, which was used in the patent to characterise the strain of the invention. The mushrooms sold by the defendants had exactly the same sequence at this marker as the deposited strain, so the court held that they infringed the patent.

This case demonstrates the benefit of properly characterising a strain and discussing in the patent specification how the strain of the invention should be identified. Without such details, which are not present in many patents, the infringement case would have been much weaker. This is because, in the absence of a scientific consensus regarding how members of a strain should be identified, the court could easily have adopted the option presented by the defendants.

A comprehensive analysis and comparison was also carried out by the Norwegian Court of Appeal in *Pharmaq v. Intervet*[4], following a judgement of the EFTA Court. The EFTA Court fulfils a similar function to the Court of Justice of the EU, but for the EFTA states. Intervet and Pharmaq both made vaccines to protect salmon against viral infection, and the two vaccines used different strains of the same virus. The various decisions of the courts addressed many different issues, one of which was whether or not the two different strains of the virus constituted the same active agent. The scale of the comparisons that were submitted to and considered by the courts is striking. These culminated in numerous field studies comparing the potencies of the two vaccines at protecting salmon from infection. In the end, it was held that the vaccines did not comprise the same active agent because the

allegedly infringing vaccine was significantly more effective.

It is certainly possible that a dispute relating to a patent claim to a deposited strain and different bacterial products could develop in a similar manner to *Pharmaq v. Intervet*. In the absence of any scientific consensus about the boundary of a strain, and in the absence of clear and reasonable guidance in a patent, then opposing sides will likely analyse the differences between bacterial products, because there will always be some detectable differences. Courts will then have to establish whether the differences are minor and inconsequential or whether the differences show that there are two distinct active agents that should be seen as different strains.

The doctrine of equivalents, as established in the UK by the Supreme Court in *Eli Lilly v. Actavis*[5], should also be considered when analysing the scope of a claim to a deposited strain. The Supreme Court set out that a claim may be infringed by a variant, even if the variant is outside the literal meaning of the claims. This is interesting because it offers the possibility of a bacterial strain infringing a patent that is explicitly limited to a different strain. The Supreme Court established three requirements that must be met in order to find infringement by a variant. Firstly, the variant must achieve substantially the same result in substantially the same way. Secondly, it must be obvious the effect of the variant is achieved in substantially the same way. Thirdly, the patent must not indicate that strict compliance with the literal meaning of the claims is an essential requirement of the invention. If two bacterial strains are both used for treating the same disease, then they could be said to achieve substantially the same result in substantially the same way. Therefore, if a patent did not clearly indicate that the invention absolutely required the claimed strain, then a claim to a specific strain might be infringed by a different strain.

The Boards of Appeal of the European Patent Office recently considered the scope of a claim referring to a deposit in T32/07[6]. At first instance the Opposition Division had concluded that the claim to an antibody produced by a specific deposited hybridoma was valid. However, the Board concluded that the hybridoma deposit in question "*does not in itself convey any technical information about the molecular structure of the monoclonal antibody produced by said hybridoma, such as its amino acid sequence*", and as a result it found the relevant claim to lack novelty. The reasons for this decision relate primarily to the interpretation of product-by-process claims, but it shows that it cannot be assumed that a reference to a specific deposit in a claim will provide patentability benefits.

In practice, the value of a patent claim is heavily dependent on its commercial context. In relation to the microbiome and live biotherapeutic products, regulatory issues are likely to be highly significant. This is because only certain specific strains are approved for use in food products and cosmetics, and the same will be true of medicinal products. A patent limited to a specific strain may be very valuable in this context, because an infringer may not have the option of arguing that their strain is different from the protected strain, if their regulatory approval is dependent on the bacteria in their product belonging to the approved strain.

However, the value of a patent to its proprietor is also dependent on the nature of the commercial competition that the patent proprietor is facing. When the first live biotherapeutic products are approved, it seems very unlikely that there will be any competition from generics manufacturers. Instead, different innovator companies are likely to compete with their own products and their own strains, and the innovator companies may well be free to argue that their strain is different from a protected strain. In that context, a patent limited to a specific strain may be of less value. Instead, claims that are not limited to a specific strain will be very useful, such as claims that recite broader taxonomic classifications, perhaps in combination with metabolic and phenotypic characteristics.

In conclusion, a claim limited to a specific deposited strain is *potentially* extremely narrow, and could extend only to descendants of that deposit, based on a literal and formal interpretation. However, in *practice* such a claim is likely to be useful and potentially infringed by competitor products. The value of patents claiming deposited strains will be increased if they include details on how the strain is characterised and can be identified. Ideally, patents should also describe functional attributes of the strain of the invention, such as the metabolites that it produces or the effects it has on certain immune cells. This type of information is very likely to be useful when trying to enforce a patent against a related strain that shares those attributes. If possible, broader claims that extend to variants of a strain or to a species of bacteria are of course highly valuable, but in the increasingly congested microbiome field, such claims require comprehensive characterisation of the bacteria and careful and creative patent drafting and prosecution.

Footnotes

1. Calculated by reviewing the claims of all patents granted by the EPO in 2019 and 2020 with International Patent Classification (IPC) code A61K35/74, excluding patents that are not directed to naturally-occurring bacteria.
2. Van Rossum, et al. Diversity within species: interpreting strains in microbiomes. *Nat Rev Microbiol* 18, 491–506 (2020)
3. Shanghai Finc v. Tianjin LSPY (2017) Beijing 73 civil preliminary case No. 555, CN103503780B
4. Pharma AS v. Intervet International B.V. (2016) Borgarting Court of Appeal, 15-170539ASD-BORG/01 and 15-204605ASD-BORG/01
5. Eli Lilly v. Actavis [2017] UKSC 48
6. T32/17 – 3.3.04 – Bispecific antibody/ DIASOURCE (2020)

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