Fordham IP Conference, April 2012

Biotech and Gene Patents:

HGS v Eli Lilly

Dr Penny Gilbert

Powell Gilbert LLP

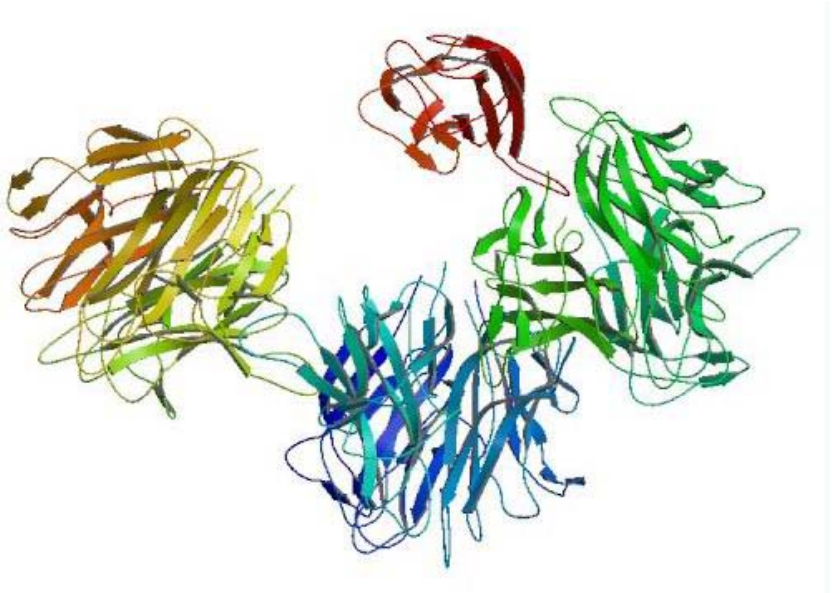
Powell Gilbert

A Health Warning:

- My comments reflect my personal opinions.

Powell Gilbert

Neutrokine α



- HGS : **EP 0 939 804** - discloses sequence of a novel member of the TNF ligand superfamily: Neutrokine α
- Identified potential uses based on the known immunomodulatory activities of the other TNF ligand superfamily members

EP (UK) 0 939 804 : claims

- Claims (as amended) include *inter alia*
  - Full length polypeptide and the Extracellular Domain of Neutrokine-α
  - Nucleic acid sequences encoding these 2 polypeptides
  - Antibodies specifically binding these polypeptides
  - Pharmaceutical and diagnostic compositions comprising the polypeptides or antibodies to Neutrokine-α

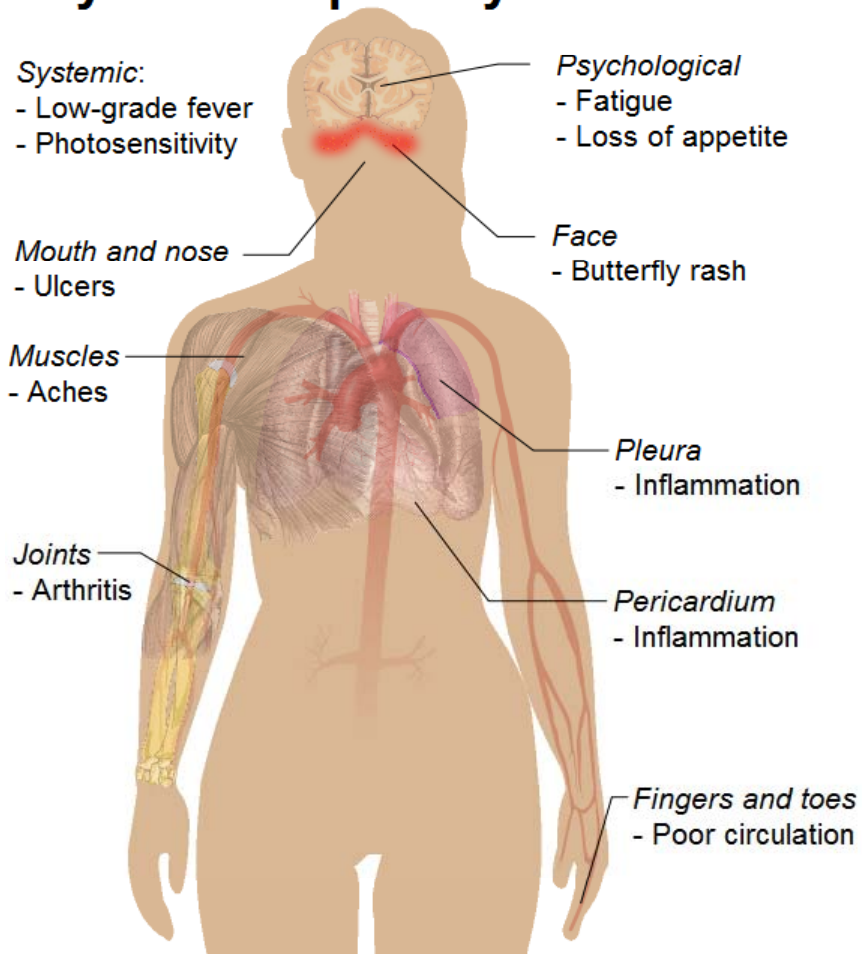
- NO USE CLAIMS.

Key Issue - Industrial Application

- First time this issue has been considered in detail by the UK courts
- Previously considered to be a low threshold for patentability (applicable to perpetual motion machines etc)
- Now a particular issue for gene patents because of the European Biotech Directive
- The protein and antibodies to it were being sold as research tools shortly after publication of the sequence
- Both parties had their own MAbs in development for treatment of immune disorders: HGS' Belimumab approved for treatment of Lupus (an autoimmune disease)

Most common symptoms of

Systemic lupus erythematosus



Powell Gilbert

IA: EPC and PA 1977

- Basis for requirement of industrial application enshrined in Article 52(1) EPC:

  "*European patents shall be granted for any inventions, in all fields of technology, provided that they are new, involve an inventive step and are susceptible of industrial application*"

- Article 57 EPC defines industrial application as:

  "*An invention shall be considered as susceptible of industrial application if it can be made or used in any kind of industry, including agriculture*"

- Section 1(c) UK Patents Act 1977:

  …"*capable of industrial application*"

Powell Gilbert

Biotech Directive

- Recitals 23 and 24 state

  "*a mere DNA sequence without indication of a function does not contain any technical information and is therefore not a patentable invention*";

  "*in order to comply with the industrial application criterion it is necessary in cases where a sequence or partial sequence of a gene is used to produce a protein or part of a protein, to specify which protein or part of a protein is produced or what function it performs*"

- Article 5(3) states:

  "*The industrial application of a sequence or a partial sequence of a gene must be disclosed in the patent application*"

Powell Gilbert

Questions:

- Purpose of the patent system is to support innovation by granting a monopoly in return for early public disclosure of the invention.
  - When is an invention fully disclosed / complete enough to justify the monopoly?
  - How much information must be disclosed?
  - Does it need to be supported by experimental proof?

UK proceedings

- At first instance, Kitchin J held no IA (but inventive over prior art clone and ESTs)
- EPO OD held obvious for lack of technical contribution, so did not decide IA
- Court of Appeal adjourned UK appeal hearing and asked EPO TBA to expedite appeal
- TBA produced decision within 10 months of OD's written decision
- Patent held valid (T18/09) applying TBA's case law on IA
- Written decision given shortly before the UK CoA hearing
- UK CoA held EP(UK) patent invalid for lack of IA
- HGS petitioned to Supreme Court
- BIA intervened in SC appeal on policy grounds

Powell Gilbert

IA – Findings of Fact

- In 1996, identification of new members of the TNF superfamily was desirable

  "*because of their apparent roles in the regulation of the immune system and inflammatory response, their possible involvement in various different diseases and so, in due course, their potential as therapeutic agents.*"

- Accepted, based on expert cross examination:
  - all members of TNF ligand superfamily:
    - were expressed on activated T cells; and
    - played a role in the regulation of T cell proliferation and T cell responses
  - the skilled person would appreciate from his CGK that Neutrokine- α activities might:
    - relate to T and B cells; and
    - play a role in the immune and inflammatory response, cancer etc

Powell Gilbert

IA – Held

High Court

- Neither the patent, nor CGK, identified any specific disease that Neutrokine-α could actually treat.

Court of Appeal

- what is required is:

  "*Sufficient specification of the function of the protein. Just describing the existence of a protein and its structure is not enough. Nor is it enough to describe the function at a high level of generality – e.g. that the compound must have a significant function biologically and so it .. may be useable to treat some sort of disease. You have to say what it is for with more particularity.*"

Supreme Court:

- Important issue of principle – resolution inevitably fact sensitive
- Unlikely that TBA and UK court received very different arguments in light of reasoning in the 2 decisions (although some witnesses different)
- "*plainly appropriate in principle, and highly desirable in practice, that [national courts and EPO] interpret the provisions of the EPC in the same way*"
- *"where the Board has adopted a consistent approach to an issue in a number of decisions it would require very unusual facts to justify the national court not following the approach*"
- Consistency of approach important for bioscience companies to be able to decide when to file patent
- BIA concerns noted

Powell Gilbert

Supreme Court (contd)

- *The disclosure of the existence and structure of Neutrokine-α and its gene sequence, and its membership of the TNF ligand superfamily should have been sufficient, taking into account the common general knowledge, to satisfy the requirements of Art 57 [in light of the principles to be extracted from the TBA case law]*

- T18/09 entirely consistent with the earlier TBA jurisprudence

- Court of Appeal did not approach the concept of plausibility consistently with the TBA jurisprudence:

  "It is not good enough to say this protein or any protein or any antibody to it probably has a pharmaceutical use. Such a statement is indeed ***plausible****, but is of no real practical use*"

- *Prima facie* this satisfies the requirement of Art 57

Supreme Court : In summary

- The fact that the members of the superfamily were known to have pleiotropic effects is irrelevant where the value of new members relates to the common features manifested by all known members

- Neither the judge nor the TBA considered the “boilerplate” drafting of the specification would have diverted the person skilled in the art from what their search of the literature, coupled with CGK, would have led them to understand was taught by the patent

- Standard set for IA by the judge was more exacting than that used by TBA – looking for whether a particular use had been demonstrated vs whether product plausibly shown to be usable (even if further research required)

Conclusions

- SC guidance that settled jurisprudence of the EPO TBAs should be followed by the UK courts to achieve harmonisation
- SC took note of policy issues and concerns expressed by BIA on behalf of biotech industry
- The IA threshold has not been elevated for gene sequence patents
- **BUT,** each case will turn on its facts:
  - Was the full length sequence disclosed?
  - Does it have the characterising domains/ features of a family?
  - Does that family have well defined functions?
  - If the family has pleiotropic functions is there a discernible "core" of activities that might plausibly lead to use?

Powell Gilbert