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# European Biotech Patent Law Update

21 May 2019

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# Webinar agenda

- New Clinical Situations
- T 433/14 – mechanism of action
- Regen Lab v Estar – equivalents
- Referrals to EBoA:
  - T 318/14 – double patenting
  - G 2/19 – OPs at Haar

# Claims to New Clinical Situations

- Is it possible to protect a mechanism of action of a drug -
  - in theory, no, as this relates to a mere ‘discovery’

- However, if the mechanism of action confers a new clinical situation, then it may be possible to obtain patent protection.

# G2/88 - Mobil

"*Under A 54(2) EPC the question to be decided is what has been "made available" to the public: the question is not what may have been "inherent" in what was made available*".

# T 0290/86 (Imperial Chemical Industries PLC)

**Claim 1:**

*"1. The use of a salt of lanthanum for the manufacture of a non-oxidising aqueous mouthwash, oral spray, toothpaste or dental gel for cleaning plaque and/or stains from human teeth...."*

**Prior art:**

- D1 discloses the use of dentifrice preparations containing lanthanum salts to depress the solubility of tooth enamel in organic acids, and thus to inhibit tooth decay.

# T 0290/86 (Imperial Chemical Industries PLC)

**Result:**

*"Although the skilled person would know that the use of a toothpaste in accordance with document (1) would, at least to some extent, remove plaque, he would not realise that the ability of the toothpaste to remove plaque is improved by the presence of lanthanum salts.*

*… in the Board's judgment the use of lanthanum salts to remove plaque and/or stains from teeth represents a further novel therapeutic application in accordance with Decision G 5/83, as compared to the previous disclosure of the use of such salts to depress the solubility of tooth enamel in organic acids."*

## Claim 1 held to be <u>novel</u> over D1

# T 0836/01 (Yeda Research and Development CO. LTD)

**Claims 1 and 2:**

*"1. Use of human interferon-ß2 for preparing a medicament for influencing tumor cell growth and differentiation.*

*2. Use of human interferon-ß2 for preparing a medicament for influencing terminal differentiation of cancer cells."*

**Prior art:**

- D1 discloses interferon-ß2 for treating cancer
- D1 discloses the use of interferon-ß2 for the purpose of activating mature lymphoid cells exerting cytolytic T cell activity on cancer cells or to stimulate the immune system of patients undergoing (cancer) radio- or chemotherapy. D1 thus teaches an indirect effect of interferon-ß2 on cancer cells.

# T 0836/01 (Yeda Research and Development CO. LTD)

**Result:**

*"the conclusion cannot be drawn that the technical effect relied upon by the claimed invention, namely the direct influence of interferon-ß2 on the tumor cell growth and (terminal) differentiation is a mere explanation of how interferon-ß2 heals cancer. Rather, this effect identifies a new clinical situation, namely one in which it could be preferable to target the cancer cells themselves, not lymphoid cells or the immune system as in document (D1), in order to heal cancer. But since a new clinical frame is not separable, as an abstract concept, from a patient suffering under it, it must be concluded that this new clinical situation also identifies a new sub-group of subjects being treated."*

## Claims 1 and 2 held to be <u>novel</u> over D1

# T 1642/06 (Spruce Barbara, et al)

**Claim 1:**

*"Use of a sigma receptor ligand for the preparation of a medicament for inhibiting neovascularisation of tumours, by modulating proliferation and/or survival of endothelial cells, wherein the sigma receptor ligand is a sigma receptor antagonist which inhibits endothelial cell proliferation and/or survival."*

**Prior art:**

- D1 discloses the use of a sigma receptor ligand (rimacazole) for the preparation of a medicament for treating tumours (breast cancer)
- D1 discloses the use of compositions for the purpose of inducing tumour cell division cycle arrest and/or apoptosis. Thus, D1 teaches a direct effect of sigma receptor ligands on cancer cells.

# T 1642/06 (Spruce Barbara, et al)

**Result:**

*"…document (1) teaches a direct effect on cancer cells. This is in clear contrast to the technical effect relied upon in claim 1, namely the indirect influence of sigma receptor ligands on tumour cells via the inhibition of the neovascularisation of tumours.*

*This effect, moreover, identifies a new clinical situation, namely one in which it could be preferable to target the supporting vasculature of a tumour rather than the cancer cells themselves, for instance in cases where the cells are resistant to chemotherapeutic drugs."*

**Claim 1 held to be novel over D1**

# T 1955/09 (Octoplus Sciences)

**Claim 1:**

*"The use of a peptidic compound for the manufacture of a medicament for the prophylactic or therapeutic treatment of a bacterial or fungal infection of a mammal by killing said bacteria or fungi, wherein the compound comprises an amino acid sequence: X1KEFX2RIVX3RIKX4FLRX5LVX6…"*

**Prior art:**

- D1 discloses the use of the same peptide for the therapy or prevention of a disease resulting from a fungal or bacterial infection.
- D1 discloses that the mechanism of action of the peptide is to inhibit or neutralise fungal or bacterial toxins.

# T 1955/09 (Octoplus Sciences)

- The board held that:

- "*the attaining of a new technical effect is considered as a functional technical feature of a claim referring to the new use of a known substance. If that technical feature has not been previously made available to the public, then the claimed invention is novel, even though such technical effect may have inherently taken place in the course of carrying out what has previously been made available to the public*".

- The Board had to decide whether the use now claimed represents a further and different therapeutic use from the disclosure in document (D1).

# T 1955/09 (Octoplus Sciences)

**Result:**

*"The conclusion can not be drawn that the technical effect relied upon by the claimed invention, i.e. the antibiotic effect, is a mere explanation of how the compounds inhibit or neutralize toxins. Rather, this effect identifies a new clinical situation, namely one in which it could be preferable to target the infection itself, not merely the toxins produced by the bacteria or fungi causing the infection."*

**Claim 1 held to be novel over D1**

# T 0433/14 (Newron Sweden B)

- Claim
- At least one agent that elevates intracellular cAMP levels in neural tissue, wherein said agent is selected from the group consisting of… Glucagon-Like Peptide-1..and Exendin-4….for use in increasing neurogenesis in neural tissue of a patient exhibiting a central nervous system disorder selected from the group consisting of neurodegenerative disorders, ischemic disorders, neurological traumas, and learning and memory disorders, wherein the agent increases neurogenesis in the patient…wherein increasing neurogenesis is increasing proliferation of an adult neural stem cell in said neural tissue".

# T 0433/14 (Newron Sweden B)

- **Prior art**

- D12 discloses "A method of treating a subject with a neurodegenerative condition or of reducing one or more symptoms of a neurodegenerative condition in a subject, comprising administering to the subject a therapeutically effective amount of a polypeptide comprising GLP-1 or exendin-4.

- D12 also discloses GLP-1 or exendin-4 for therapeutically treating a "neurodegenerative condition or [...] diseases, including, for example, Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, multiple sclerosis, and peripheral neuropathy", ischemic disorders ("stroke"), neurological traumas ("brain or spinal cord injury"), and learning and memory disorders (cf. Alzheimer's disease).

# T 0433/14 (Newron Sweden B)

- **Proprietor's arguments**
- Proprietor argued that D12 focused on neuronal precursor cells and not neuronal stem cells.
- No proliferative effect of the claimed agents was demonstrated in D12.
- D12 disclosed only a neuroprotective effect, i.e. a mechanism through which neurons are protected from damage. This effect could not result in the generation of new neurons.
- In contrast, the neurogenesis effect disclosed in the patent allowed regenerative therapy which could replace lost or damaged neurons.
- Thus, the claimed agents were for use in a new clinical situation, i.e. in the treatment of a group of subjects (patients) distinguishable from those treated according to document D12.
- The new patient group consisted of those patients for whom neuroprotective treatments would be ineffective, i.e. those who were at a disease stage where neurons had already been destroyed.
- Examples of patients who could benefit were those suffering from ischemic disorders such as stroke or neurological trauma, where there was sudden and essentially complete loss of neurons.

# T 0433/14 (Newron Sweden B)

- **Decision**

- "*The board is of the view that the above mentioned physiological effects inherently occur when treating subjects in accordance with the relevant disclosure of document D12. In other words they describe a mechanism for the treatment disclosed in document D12. These features therefore cannot serve to differentiate the claimed subject-matter from that disclosed in document D12*."

- " *It is therefore of no consequence to the novelty of the claimed subject-matter that there may exist a patient group that could benefit from the claimed invention but not from the therapeutic treatment disclosed in document D12, because the claimed subject-matter is not directed to such a group*. "

# T 0433/14 (Newron Sweden B)

- "*Such a situation also underlay the considerations in decision T 406/06. Here the board, in a different composition, noted that "it is not stated in G 5/83 that novelty of a therapeutic use can be established merely on the basis of a new technical effect" and that "in interpreting decision G 5/83, the boards of appeal have [...] ruled that a new technical effect alone is not sufficient to establish novelty of a second medical use, but that a therapeutic use may only be considered as novel if the new technical effect also leads to a truly new industrial/commercial application or activity*"

# Lessons

- May need to explicitly define the patient subgroup in the claim, rather than relying solely on the mechanism of action.

- If no explicit basis in application for defining patient sub group, relying on common general knowledge or prior art to justify that a skilled person could readily identify such patients may not remedy the deficiency.

# Regen Lab v Estar

- Regen Lab SA v Estar Medical Ltd & Ors [2019] EWHC 63 (Pat)
- Infringement of a “numerical claim” as an equivalent
- Application of *Actavis* questions

# Background

- Actavis UK Ltd and others v Eli Lilly and Company [2017] UKSC 48
- Reformulated the UK courts' assessment of patent infringement
- Effectively introduced a doctrine of equivalents
- Separation of "normal" interpretation and infringement by variants – fundamental change to claim interpretation in the UK
- Two-step approach considered to be more in line with the Protocol on the Interpretation of Article 69 of the European Patent Convention (EPC)

# *Actavis* questions

1. Does the variant infringe any of the claims as a matter of normal interpretation?

2. If not, does the variant nevertheless infringe because it varies from the invention in a way or ways which is or are immaterial? This is to be determined by asking these three questions:

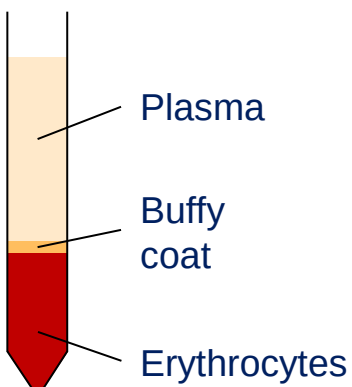
a) Notwithstanding that it is not within the literal meaning of the relevant claim(s) of the patent, does the variant achieve substantially the same result in substantially the same way as the invention, i.e. the inventive concept revealed by the patent?

b) 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 does so in substantially the same way as the invention?

c) 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?

# Regen Lab v Estar

- EP(UK)2073862 – Method for the preparation of blood plasma enriched in platelets and other factors (platelet-rich plasma, PRP)
- Therapeutic uses of PRP in wound or tissue healing, or regeneration treatments
- PRP prepared by centrifugation:
  - Erythrocytes – pellets
  - Leukocytes and platelets – middle layer
  - Plasma – supernatant



# Claim 1

A process for the preparation of a cell composition, comprising the steps of:

(a) Centrifuging whole blood in a separator tube selected from:

- a glass separator tube containing a polyester-based thixotropic gel and a buffered sodium citrate solution at 0.10 M; and

- a polyethylene terephthalate separator tube containing a highly thixotropic gel formed by a polymer mixture and an anhydrous sodium citrate at 3.5 mg/mL;

(b) Separating enriched platelet rich plasma from full plasma by removing about half of the supernatant containing platelet poor plasma;

(c) Re-suspending the enriched plasma;

wherein the centrifugation step a) is performed at a force of or about 1500g up to about 2000g in a sufficient length of time to form a barrier between plasma containing platelets, lymphocytes and monocytes and a pellet containing erythrocytes; the separation step b) is made by collecting the supernatant from atop of said barrier and wherein the enriched plasma is enriched in leucocytes, thrombocytes and adhesion proteins as compared to native whole blood.

# Validity

- Patent found to lack novelty and inventive step
- Public disclosure of the claimed method by Regen’s witness
- Having found the patent invalid, HHJ Hacon then turned to assessing infringement

# Infringement – Claim 1

A process for the preparation of a cell composition, comprising the steps of:

(a) Centrifuging whole blood in a separator tube selected from:

- a glass separator tube containing a polyester-based thixotropic gel and a buffered sodium citrate solution at 0.10 M; and

- a polyethylene terephthalate separator tube containing a highly thixotropic gel formed by a polymer mixture and an anhydrous sodium citrate at 3.5 mg/mL;

(b) Separating enriched platelet rich plasma from full plasma by removing about half of the supernatant containing platelet poor plasma;

(c) Re-suspending the enriched plasma;

[…]

# Infringement

- Estar’s case on non-infringement was:
  1. The thixotropic gel of their product was not polyester-based
  2. Their sodium citrate solution was at 0.136 M, not “0.1 M”

- Regen’s main argument on infringement was based on equivalence

# Infringement

- HHJ Hacon found Estar's process fell outside the claims under normal interpretation – Estar's gel was not polyester-based
- Moved on to apply the principles of claim interpretation set out by *Actavis v Eli Lilly* (reviewed by the Court of Appeal in *Icescape v Iceworld*)
- Specific issues of law arose on the question of equivalence which are of wider relevance:
  - Application to variants with multiple differences
  - Application to numerical claims

# Multiple differences

- Should multiple differences between the alleged infringement and the claim be assessed separately or with all differences taken together?

- If there is some interaction between the relevant elements, there could be different answers depending on how the equivalents are considered

# Multiple differences

- “The question is whether the accused product or process is a variant falling within the scope of the claim taking all equivalents into account. Of course, it will often be convenient to consider equivalents one by one, but there must be a single overall answer in relation to each accused product or process.”

# Numerical claim

- Estar argued that the doctrine of equivalents could not apply to numerical claim

- “[T]he approach to claims containing one or more numerical limits […] is no different to that applicable to any other claim. I do not believe that *Actavis* has changed that.”

# *Actavis* – Question 1

- Notwithstanding that it is not within the literal 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, i.e. the inventive concept revealed by the patent?

# *Actavis* – Question 1

- Inventive concept:

  > "[…] the preparation of PRP for solely therapeutic use by employing a thixotropic gel wherein (a) there is only one centrifugation and (b) after centrifugation about half the supernatant is removed and the platelets are then re-suspended in the enriched plasma."

- Estar's own expert suggested that neither of the two differences in Esta's process mattered in relation to the process

# *Actavis* – Question 1

- Key property of the gel is its density
- Molarity of sodium citrate per se is not important
- HHJ Hacon found that the precise gel and buffer compositions were not part of the inventive concept
- Changing these compositions made no difference to the exploitation of the invention
- Question 1: YES

# *Actavis* – Question 2

- 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 does so in substantially the same way as the invention?

- Question 2: YES

# *Actavis* – Question 3

- 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?

# *Actavis* – Question 3

- Before *Actavis*, purposive construction did not mean that an integer could be ignored if it did not appear to make any difference to the inventive concept
- However, the focus should now be on the “inventive concept” and not on the claim language
- Following *Actavis* the patent appears to protect more than the claimed invention – it protects the inventive concept

# *Actavis* – Question 3

- Estar argued that the reasons concluding that a product or process falls outside a numerical claim on normal construction would necessarily drive the skilled person to the view that the patentee intended that strict compliance with the relevant numerals is an essential requirement of the inventive concept

# *Actavis* – Question 3

- HHJ Hacon:
  - "I disagree. First, it would put numerical claims into a special class: the doctrine of equivalence does not apply to them."
  - "Secondly, the normal construction of a claim may be narrower than the purposive construction according to *Kirin-Amgen*, so if [the Defendant] were right the effect of *Actavis* could be to narrow the scope of numerical claims, which I believe would run contrary to the intention underlying the Supreme Court's judgment."

# *Actavis* – Question 3

- “I do not take the view that the doctrine of equivalence is to be disapplied to numerical claims.”

- “I accept that the use of the extra decimal place, 0.10M rather than 0.1M, is relevant, although I think it relates to the question whether 0.10M can be stretched to cover 0.136M as a matter of normal construction rather than the question of equivalence.”

# *Actavis* – Question 3

- “The evidence indicated that the molarity of the sodium citrate is not essential to the inventive concept and would not have been so regarded by the skilled person at the priority date.”

- Question 3: NO

- If the patent had been valid, it would have been infringed

# Summary

- UK courts may find infringement despite clear numerical limitations in the claim not being satisfied.

- What happens when it is the integers in the claim that render the entire claim novel?

- Prosecution estoppel arguments may be difficult to succeed on.

# Referrals to EBoA

- T 318/14 – double patenting
- G 2/19 – OPs at the Haar

# T 318/14

- Referral from T 318/14 – double patenting
- Prohibition of double patenting based on *obiter* comments in G 1/05 and G 1/06
- Based on the notion that an applicant has no legitimate interest in proceedings leading to the grant of a second patent for the same subject-matter if he already possesses one granted patent for that subject-matter
- BoA recognised conflicting case law

# T 318/14

1. Can a European patent application be refused under Article 97 (2) EPC if it claims the same subject-matter as a European patent granted to the same applicant which does not form part of the state of the art pursuant to Article 54 (2) and (3) EPC?

2.1. If the answer to the first question is yes, what are the conditions for such a refusal and are different conditions to be applied where the European patent application under examination was filed

a) on the same date as, or

b) as a European divisional application (Article 76 (1) EPC) in respect of, or

c) claiming the priority (Article 88 EPC) in respect of a European patent application on the basis of which a European patent was granted to the same applicant?

# T 318/14

2.2. In particular, in the latter case, does an applicant have a legitimate interest in the grant of the (subsequent) European patent application in view of the fact that the filing date and not the priority date is the relevant date for calculating the term of the European patent under Article 63 (1) EPC.

# G 2/19

- Referral from T 831/17 – validity of decisions in Haar
- BoAs moved from EPO buildings in Munich to offices in Haar
- Appellant argued that holding OPs in Haar not in conformity with EPC
- OPs for T 831/17 moved on the day to Munich and questions referred to EBoA: can the Board hold oral proceedings in Haar without violating Article 116 EPC?
- Potential delay to proceedings
- Question over whether decisions issued in Haar might be invalid

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