European and US Patent Strategies for Cell Therapies

Martin MacLean & Craig Titmus

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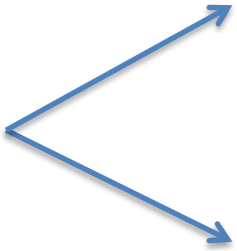
European and US Patent Strategies for Cell Therapies

- Common European and US patentability requirements
- Cell therapy patenting in Europe
  - Historic case law
  - Stem cells
  - Practical advice
- Cell therapy patenting in the US
  - Historic case law
  - Interim USPTO guidance
  - Worked example
  - Outlook
  - Practical advice
- Questions

Common European & US patentability requirements

- Established criteria
  - Novel
  - Inventive
  - Industrially applicable

- Organic criteria
  - Responsive to case law



Europe
(Morality & enablement – part of a "tiered" assessment)

US
(Patent eligibility – overriding effect)

Cell therapy patenting in Europe

- Stable legal landscape & reasonably predictable Examiners
- Established patentability objections
  - Method of treatment by surgery or therapy
  - Diagnostic methods performed on the human or animal body
  - Lack of novelty
  - Technical effect not “plausible”, particularly for therapeutics
- Established solutions
- Organic objections based on case law – esp. stem cells

Historic European case law

G2/06 "the WARF decision" (2009)

- Not patent eligible if claims are directed to products which, at the filing date, could be prepared **exclusively** by a method **necessarily** involving the destruction of **human embryos**, even if the method is not part of the claims.

Brüstle v. Greenpeace (2012)

- Defines a "human embryo" as:
  - fertilized human ovum; and *". . . non-fertilised human ovum whose division and further development had been **stimulated by parthenogenesis**. … **capable of commencing the process of development of a human being** just as an embryo created by fertilisation of an ovum can do so."*

Stem cell patenting in Europe

(a) Induced pluripotent stem cells – *always been patent eligible*

- Generated directly from adult somatic cells = outside of case law exclusions

(b) Human parthenogenetic stem cells – *patentability status update*

- Derived from parthenogenetically activated human oocytes (via stimulation of unfertilized oocytes)
- Previously classified as a "human embryo" due to being "*capable of commencing the process of development of a human being*" (Brüstle)

(c) Human embryonic stem cells – *patentability status update*

- Clearly relates to human embryos (cannot claim embryos *per se*)
- Excluded if claims require *"prior destruction of human embryos"* (WARF)

Human parthenogenetic SCs

Historically not patent-eligible

In Dec '14, the CJEU held in the "ISCC" case that:

- *"unfertilized human ovum whose division and further development had been stimulated by parthenogenesis does not constitute a 'human embryo"*

(International Stem Cell Corporation v. Comptroller General of Patents, CJEU, 2014)

- Scientific advancement:
  - Parthenotes **cannot** develop into viable human beings *[they lack paternal DNA necessary for the development of extra-embryonic tissue]*

New patentability status: human parthenogenetic SCs are now patent-eligible

Human embryonic SCs (i)

- Inventions which use human embryos for industrial or commercial purposes are considered unethical and are not patentable in Europe

- Inventions using hES cells from *established cell lines* can be permitted:

  *"Inventions which rely on the use of established hES cell lines which were initially derived by a process resulting in the **destruction** of a human embryo are **excluded from patentability…** even if the de novo destruction of human embryos is not encompassed by the invention"*

  (Technion Research and Development Foundation 04.02.2014)

- Cut off date = when non-destructive (morally acceptable) techniques became available.

- Until very recently, the cut-off date was February 2008
  - (Chung *et al*. Feb 2008. Cell Stem Cell, Vol. 2, Issue 2, 113-117, 7)

Human embryonic SCs (ii)

- Flowing from the ISCC parthenotes case (above), the new cut off date is **5 June 2003**
  - CJEU determined that that parthenotes are not human embryos, so the use of parthenotes to obtain hESCs is (now) morally acceptable
  - WO03/046141 (published 5 June 2003) discloses methods of deriving hESCs from parthenotes - the skilled person would have been able to generate parthenotes and derive hESCs from 5 June 2003

Practical advice - Europe

- Check for recent refusal of SC-related cases
  - If filed after 5 June 2003, then consider appeal
- Inventive Step – ensure that technical effect is "at least plausible"
  - Admission of post-filed data to support inventive step
- Novelty
  - Mere "isolation" is enough to establish novelty over nature
  - Product-by-process claims - look for process "fingerprints"
  - New therapies (involving known product) – remember product *per se* claims
    - Features required for new use *e.g.* aerosol, solid/liquid, lyophilised *etc.*)

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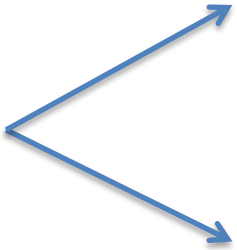

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Cell therapy patenting in the US

- Legal landscape is unstable
  - Disruptive Court and Federal Circuit decisions (Prometheus & Myriad)
- USPTO is struggling to implement changes consistently
  - Unpredictable Examiners
- Interim examination guidelines have been issued (Dec '14)
  - Discussed below

Historic US patent-eligibility case law

Natural products and natural principles are not patentable

- *Association for Molecular Pathology v. Myriad Genetics, Inc:*
  - Esp. product claims
  - Case related to the BRCA1/2 genes
  - cDNAs held patent eligible, but not isolated DNAs

- *Mayo Collaborative Services v. Prometheus Laboratories, Inc*
  - Esp. process claims
  - Case related to a diagnostic test
  - "Pure" diagnosis based on natural correlation held not patent eligible

Interim USPTO Guidance on Subject Matter Eligibility

- Issued by the USPTO (responsive to complaints from patent bar)
- Intended to assist Examiners and the public in determining whether a claim is patent-eligible, in view of recent U.S. Supreme Court decisions
- *[Interim guidance issued Dec '14 with accompanying examples; public consultation led to a Jul '15 update to help provide further clarification]*

Two step analysis for determining patent-eligible subject matter

Step A

Is the claim directed to a judicial exception (*i.e*. not **markedly different** from nature)?

[Markedly different = more than an incidental or trivial difference]

If “yes”, then proceed to Step B…

Step B

Does the claim recite additional elements that amount to **significantly more** than the judicial exception?

USPTO's Illustrated Example

Scenario:

- Patent application discloses a method for differentiating target cells into pacemaker-like cells, for use in regenerating damaged heart tissue

- Background on natural pacemaker cells:
  - They express marker P on their surface
  - They *encode* marker Z, but marker Z is never expressed in nature

USPTO's Illustrated Example

Applicant's method provides a mixed population of cells:

- Some **genetically and phenotypically identical** to natural pacemaker cells
- Some genetically identical, but have a **different phenotype**: they express marker Z and use oxygen more efficiently (**= useful in therapy**)

Additional observations in the patent application:

- The **mixed population** of pacemaker cells is 10-15% positive for marker Z and 85-90% positive for marker P, and causes the marker P cells to **grow faster**
- The mixed cell population can be combined with a **naturally-occurring** "biocompatible, three-dimensional scaffold". This allows the cells to be directly implanted into a patient, providing faster tissue regeneration than when implanted by themselves (**= useful in therapy**)

USPTO's Illustrated Example – Hypothetical claim 1 (of 5)

Claim 1: **An isolated man-made human pacemaker cell**

Step A: *Do the cells possess "markedly different" characteristics from a naturally occurring human pacemaker cell?*

No - proceed to Step B

***Step B**: Does the claim include any additional features that could add significantly more to the judicial exception?*

No – Claim 1 is not patent-eligible

[NB: Some of the man-made cells are identical to the natural counterpart cells]

USPTO's Illustrated Example – Hypothetical claim 2 (of 5)

Claim 2: **An isolated man-made human pacemaker cell expressing marker Z**

Step A: *Do the cells possess "markedly different" characteristics from a naturally occurring human pacemaker cell?*

Yes – no need to proceed to Step B

Claim 2 is patent-eligible

[NB: No natural counterpart, and Z cells use oxygen more efficiently]

USPTO's Illustrated Example – Hypothetical claim 3 (of 5)

Claim 3: **A population of human pacemaker cells, where the population is about 10-15% positive for marker Z, and 85-90% positive for marker P**

Step A: *Do the cells possess "markedly different" characteristics from a naturally occurring human pacemaker cell?*

Yes – no need to proceed to Step B

Claim 3 is patent-eligible

[NB: When mixed in this ratio, the P cells have an increased growth rate]

USPTO's Illustrated Example – Hypothetical claim 4 (of 5)

Claim 4: **A composition comprising a population of isolated man-made human pacemaker cells in a container**

Step A: *Do the cells possess "markedly different" characteristics from a naturally occurring human pacemaker cell?*

No - proceed to Step B

Step B*: Does the claim include any additional features that could add significantly more to the judicial exception?*

No – Claim 4 is not patent-eligible

[NB: No indication that placing the cells in a generic container results in the cells having any characteristics (structural, functional, or otherwise) that are different from the naturally occurring cells in their natural state]

USPTO's Illustrated Example – Hypothetical claim 5 (of 5)

Claim 5: **A composition comprising a population of isolated man-made human pacemaker cells in a biocompatible three-dimensional scaffold**

Step A: *Do the cells **or scaffold** possess "markedly different" characteristics from a naturally occurring human pacemaker cell **or scaffold**?*

No indication that they do - proceed to Step B

***Step B**: Does the claim include any additional features that could add significantly more to the judicial exception?*

Yes – the combination provides synergistic advantages, so claim 5 is patent-eligible

[NB: Directed to a combination of natural products – a population of isolated cells and a biocompatible scaffold. Combination gives therapeutic benefits]

Outlook in the US

- *Interim Guidance* example finds that many cell technologies are patent-eligible
- Mere "isolation" or reference to "man-made" is not enough
- A nature-based product is patent-eligible if it possesses any characteristic (structural, functional or otherwise) that is "markedly different" from its natural counterpart, *i.e.* more than a trivial or incidental difference
- A combination of features may render a claim patent-eligible if it provides an in use (synergistic) effect that is "significantly more" than the judicial exception itself

Practical advice - US

- "Markedly different" (avoids consideration of "significantly more")
  - Structure (*e.g.* markers, cell populations, different chemistry)
  - Property (*e.g.* different or improved characteristics)
  - Consider expert declarations (+ data) establishing markedly different characteristics
- "Significantly more"
  - Ensure that new applications recite combinations delivering "significantly more" (synergistic) technical effects
- Interview USPTO Examiners

Any questions?

Strategic advice to help your business grow.

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