Human Embryonic Stem Cells and the European Exceptions from Patentability

- European Pharmaceutical Law, IPR & the Life Sciences - Lecture VI

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Product development phase: where are we?

Research

- Research for drug targets & chemical entities
- Pre-clinical
  - Animal testing phase 1-3

Development

- Clinical Trials
  - Phase 1
    - 20-100 Healthy humans
    - 5 patients
  - Phase 2
    - 100-500 patients
  - Phase 3
    - 1000-5000 patients

Approval

- Registration process
- Market authorisation (MA)
- Government pricing and reimbursement negotiations
- Commercialisation

Life

- Phase 4
- Continued monitoring (Pharmaco vigilance)

Generic

- Application for abridged approval of generic
- SPC: 5 years max

Develop. Phase: 10-15 years; avar. 12

Patent Protection: 20 years

Data exclusivity: 10 years (8+2+1)
Agenda

- **Ridiculously simple scientific intro**
- **EU & EPC legal framework**
- **Brüstle’s patent and national procedural history**
- **The AG’s opinion and the CJEU’s judgment**
- **What about the the EPO? - WARF**
- **How did the German BGH deal with Brüstle (...Impact on patent practice...)**
- **The CJEU corrects itself in ISCC.**
- **Conclusions & readings for next lecture**
Classical definition of a stem cell requires two properties:

- **Self-renewal:**
  - the ability to go through numerous cycles of cell division while maintaining the undifferentiated state.

- **Potency:**
  - the capacity to differentiate into various specialized cell types.
  - In the strictest sense, this requires stem cells to be either totipotent or pluripotent.
  - **but** multipotent or unipotent progenitor cells are sometimes referred to as stem cells.
Potency specifies differentiation potential

- **Totipotent** (omnipotent) stem cells: can differentiate into embryonic and extra-embryonic cell types. Can construct a complete, viable organism.

- **Pluripotent** stem cells: descendants of totipotent cells. Can differentiate into nearly all cells (can be derived by e.g. blastomere separation of hESC).

- **Multipotent** stem cells can differentiate into a number of cells, but only those of a closely related family of cells.

- **Oligopotent** stem cells can differentiate into only a few cells, such as lymphoid or myeloid stem cells.

- **Unipotent** cells can produce only one cell type, their own, but have the property of self-renewal, which distinguishes them from non-stem cells.
Basic Sources of hESC (non exhaustive list)

1) “Naturally” fertilised eggs (Brüstle)- “Surplus” embryos from fertility treatment, or fertilized eggs especially created for research purposes,

- toti-or pluripotent
- source issue raises moral concern, "embryo" is normally (not always) destroyed

2) Embryos created using therapeutic cloning/somatic cell nuclear transfer (Dolly-method) and pluripotent stem cells by parthenogenesis, i.e. stimulating an unfertilised ovum to begin dividing and developing

- tissue compatible & highly potent
- misuse of cloning techniques, may (?) fall under broad definition of human embryos, additional moral concerns with e.g. chimeras.
- What about pluripotent SCs created by parthenogenesis that can not develop into a human being??

3) Adult and foetal stem cells- from aborted foetuses, the placenta, umbilical cord blood, bone marrow, etc.

- normally less potent, but
- less ethical concerns & recent advances with

4) Human induced pluripotent stem cells (iPSCs) – Can they replace hESCs?

- somatic/adult cells artificially reprogrammed to become “pluripotent”
- safety issues & potential?
(Potential) Uses

Potential uses of Stem cells

- Stroke
- Traumatic brain injury
- Learning defects
- Alzheimer's disease
- Parkinson's disease
- Baldness
- Blindness
- Deafness
- Missing teeth
- Wound healing
- Bone marrow transplantation (currently established)
- Spinal cord injury
- Osteoarthritis
- Rheumatoid arthritis
- Amyotrophic lateral sclerosis
- Myocardial infarction
- Muscular dystrophy
- Diabetes
- Multiple sites: Cancers
- Crohn's disease
# Types of stem cells and their current uses: short summary

*Last updated 30 August 2012*

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<thead>
<tr>
<th>Stem cell type</th>
<th>Where do we get them?</th>
<th>What can they do?</th>
<th>Current research uses</th>
<th>Ready for the clinic?</th>
<th>Advantages</th>
<th>What we don’t know yet: Limitations and questions</th>
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<tr>
<td><em>Embryonic stem cells</em> (ESCs)</td>
<td>Early stage embryo called a blastocyst</td>
<td>Make all the different types of cells in our body</td>
<td>Understanding how our bodies develop from a fertilized egg; Investigating how to produce different types of specialised cell</td>
<td>The first clinical trials are now beginning; focussed on treating eye disorders; these are early stage safety trials.</td>
<td>Can produce all the different types of cells in the body</td>
<td>Still learning how to fully control differentiation of these cells &lt;br&gt; Some groups have concerns on ethical or religious grounds</td>
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<tr>
<td>Tissue stem cells (e.g. skin, blood)</td>
<td>Tissues of the adult body</td>
<td>Make only the types of cells that belong in their own tissue, e.g. skin stem cells make only types of skin cells, they do not make brain or blood cells</td>
<td>Understanding how adult tissues are made and maintained; Improving our understanding of diseases affecting adult tissues, including cancer</td>
<td>Skin and blood stem cells have been in use for a number of years for skin grafts and bone marrow transplants</td>
<td>Already partly specialised, which can make it more straightforward to obtain the particular specialised cell type required</td>
<td>Still learning how to multiply, control and use different types of tissue stem cells &lt;br&gt; <em>Treatments for blood diseases, severe burns and some types of corneal damage have been proven</em>; no other treatments are yet proven &lt;br&gt; Tissues must be ‘matched’ or come from the patient’s own body for use in treatments &lt;br&gt; Claims that stem cells from the bone marrow can produce new heart cells have been proven wrong, but research is ongoing to investigate other possible beneficial effects of these cells on the heart and other tissues</td>
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Read our full fact sheets for more detailed information on current stem cell research: [www.eurostemcell.org/factsheets](http://www.eurostemcell.org/factsheets)
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<td><strong>Umbilical cord blood stem cells</strong>&lt;br&gt;(a type of tissue stem cell)</td>
<td>The umbilical cord after the birth of a baby</td>
<td>Make the different types of cells found in the blood</td>
<td>Understanding how blood stem cells work. Mainly used to treat children with blood disorders, primarily leukaemia; although adults can sometimes be treated, this is limited because only a small number of stem cells can be obtained from a cord. Not yet proven for any other applications.</td>
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<td><strong>Mesenchymal stem cells</strong>&lt;br&gt;(a type of tissue stem cell)</td>
<td>Bone marrow</td>
<td>Make cells of the skeletal tissues: bone, cartilage, fat</td>
<td>Understanding how these cells contribute to making and maintaining tissues. Some clinical trials are underway for cartilage and bone repair, for supporting repair of blood vessels after heart attacks, and for other unrelated treatment types. Mesenchymal stem cells can be easily obtained from the bone marrow of patients. MSCs can be used for efficient generation of skeletal tissues in the body. Cells from a variety of sources. MSCs – it has not been established whether these cells are all the same. The use of MSCs by introducing them into the body’s blood system is not straightforward, evidence that they are incorrect tissue and survive/function; beneficial effects are under study.</td>
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<td>Induced pluripotent stem cells (IPS cells)</td>
<td>Made in the lab from specialized adult cells, for example skin cells</td>
<td>Behave very like embryonic stem cells - make all types of cells in the body</td>
<td>Can be made from patients and used to produce cells that act as a model “disease in the laboratory” for studying diseases and testing new drugs</td>
<td>Not yet!</td>
<td>Could provide patient-specific treatment</td>
<td>Not yet established how reprogramming works. Properties of cells need further comparison with embryonic stem cells. As with ES cells, we are still learning how to fully control these cells to ensure they make the cells we want in a way that will be safe for clinical use.</td>
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www.eurostemcell.org
Multiple layers of debates over hESCs

• **Legal, ethical and regulatory issues**
  - No consistency in regulation of hESC research (Europe, US & Global)
  - May concern (1) operation of hESC-research as such, (2) creation of new hESC cell lines & (3) requirements for funding of hESC research

• **Availability of PATENTS to protect investments in research (focus)**
  - Different approaches EU & US etc.
  - Morality clause in European Patent Law
  - Harmonization through EU Biotech Directive?

• **Special focus of this presentation**: Patent eligibility
  (no other patent criteria)
LEGAL FRAMEWORK IN EUROPE
Patents must be available for any inventions in all fields of technology, without discrimination as to the place of invention or to the place of production – if the usual patent criteria are met.
Art. 27 (2) TRIPS

(WTO) Members may exclude from patentability inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect ordre public (public policy) or morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment, provided that such exclusion is not made merely because the exploitation is prohibited by their law.
Art. 5 in EU-Directive 98/44/EC (Biotech Directive)
[cf. Rule 29 (1) & (2) EPC = Sec. 1a (1) GPA]

(1) The human body, at the various stages of its formation and development, and the simple discovery of one of its elements, including the sequence or partial sequence of a gene, cannot constitute patentable inventions.

(Thus embryos and totipotent hESC excluded)

BUT

(2) An element isolated from the human body or otherwise produced by means of a technical process, including the sequence or partial sequence of a gene, may constitute a patentable invention, even if the structure of that element is identical to that of a natural element.

(Pluripotents hESC ????)

(3) ..........specific industrial application for isolated DNA/genes......
The morality clause in the Biotech Directive

**General exception:**

- **Article 6(1)** Inventions shall be considered unpatentable where their commercial exploitation would be contrary to ordre public or morality; however, exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation.

**Specification:**

- **Article 6(2)** On the basis of paragraph 1, the following, in particular, shall be considered unpatentable:...(c) uses of human embryos for industrial or commercial purposes.
  
  - Generally accepted rule: excluded only if this being the only possible (claimed) use.
  
  - Pluripotent hESC?
EU Biotech Directive: However patentable (Exception from exception)

- (rec. 42) ...whereas in any case such exclusion does not affect inventions for therapeutic or diagnostic purposes which are applied to the human embryo and are useful to it

- restrictive interpretation
**General exception:**

**Art. 53 EPC** [cf. Art. 27 (2) TRIPs & 6.1 Biotech Dir.]

European patents shall not be granted in respect of:

(a) inventions the commercial exploitation of which would be contrary to "ordre public" or morality; such exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation in some or all of the Contracting States;

**Specification:**

**Rule 28** (cf. Art. 6.2 Biotech Directive)

Under Article 53(a), European patents shall not be granted in respect of biotechnological inventions which, in particular, concern the following:

.....

(c) uses of human embryos for industrial or commercial purposes;
• **EU Directive 2004/23/EC** on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of *human* tissues and cells – *explicitly applicable also to adult and embryonic stem cells* – *also to products derived from human embryonic pluripotent stem cells*

• **Regulation (EC) No. 1394/2007** on advanced therapy medical products – indicates that commercialization of medical products derived from human cells, such as embryonic stem cells, *in principle allowed* – but MS may prohibit it (mainly safety concerns).
Unsolved questions

• Various ethical/moral/philosophical/religious views on beginning of human life → No decision by legislators what constitutes human embryo

• Directive was developed pre-WARF (legislators did not foresee techn. develop.)

• Different understandings of what constitutes an embryo and what is meant by its use for industrial and commercial purposes (different views in MS and ECHR)

• Recitals 2, 3, 16, 37, 38 & 42 describe background, but lack more specific definitions
  - Highlight importance of harmonisation & encouraging investment
  - Clarify that processes for producing chimera, totipotent cells of humans and animals & commercial/industrial uses of human embryos are excluded from patentability. (excl.: uses “helping” the embryo)
  - What about pluripotent stem cells?

• National Courts and ultimately the CJEU had to answer a series of questions on the meaning of "human embryo":
The legal status of the embryo

- Convention on Human Rights and Biomedicine (Oviedo)
  - **Article 18 - Research on embryos in vitro**
    1. Where the law allows research on embryos in vitro, it shall ensure adequate protection of the embryo.
    2. The creation of human embryos for research purposes is prohibited.

- **Ratifications**
- **Signatures**
How Europe’s ethical divide looms over biotech law and patents, Nature 2012, 392 ff.

### Figure 1 Duty of Care versus Sanctity of Life: The European Picture

<table>
<thead>
<tr>
<th>Country</th>
<th>Strong 'care'</th>
<th>Moderate 'care'</th>
<th>Moderate 'sanctity'</th>
<th>Strong 'sanctity'</th>
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The Brüstle v. Greenpeace saga
• Mr Brüstle, had invented a way to produce, from pluripotent embryonic stem cells, specialized cells useful for developing treatments against neurological diseases such as Parkinson's.

• Blastocyst forms ca. 5 days after fertilization of human ovum
  - Cells obtained from inner cell mass of a blastocyst are pluripotent (potential to differentiate into any cell type but – at least in this case - embryo destroyed)
  - In contrast to totipotent cells preceding blastocyst formation, pluripotent cells cannot develop into a complete organism
The Brüstle case – national proceedings I

- 1997: Filed German patent application (DE19756864 C1 of April 29, 1999)

“Neural precursors, method of production and use for therapy of neural defects”

- **Claims:**

1. isolated, purified precursor cells with neuronal or glial characteristics from embryonic stem cells containing at most about 15% of primitive embryonic and non-neural cells, ..... *obtainable using ESCs* (the patent then cites a series of steps including culturing and separation)

5. Cells according to one of the Claims 1-4, whereby the embryonic stem cells from oocytes are obtained after a nuclear transplantation

- **Base material** – human embryonic pluripotent SC legally imported from Israel
The Brüstle case – national proceedings II

- Greenpeace challenged the patent (nullity suit)

  **Arg.** violates the *ordre public* or morality provision in **German Patent Law Section 2(2) No.1 to 4 PatG: No.3**:  
  
  *patents shall not be granted for the use of human embryos for industrial or commercial purposes (= Art 6(2) (c) Biotech Directive)*

- Federal Patents Court (BPatG) invalidated patent insofar as relating to precursor cells derived from hESCs

- On Appeal, BGH stayed proceeding and referred the following questions on interpretation of Biotech Directive to CJEU (under Art. 267 TFEU)
Questions referred to CJEU

1. **What is the meaning of “embryo” in Art 6(2) Biotech Directive?**
   - Does it include all stages of development of human life from fertilisation or must a certain stage of development have been reached?
   - Does it include certain cloning methods to produce totipotent cells? -- Are stem cells obtained from human embryos at the blastocyst stage always included?

2. **What is meant by the use of human embryos for industrial or commercial purposes?**

3. **What if the use of human embryos doesn’t form part of the technical teaching claimed within the patent, but is a necessary precondition for the application of that teaching?**
The opinion of AG Yves Bot (March 2011)

- Primary goal of Biotech Directive: harmonisation of national patent laws. Thus common understanding on concept of embryo should be achieved.

- Applied broad definition of embryo “from the fertilisation stage to the initial totipotent calls and to the entire ensuing process of the development and formation of the human body”.

- Pluripotent cells have no capacity to develop into human embryo. Therefore they should not fall into the definition of an embryo.

- Pluripotent cells should only be regarded as patentable if they can be obtained without detriment to embryo.

- With regard to Art. 6 (2)(c) Biotech Directive: “An invention must be excluded from patentability where the application of the technical process for which the patent is filed necessitates the prior destruction of human embryos or their use as base material, even if the description of that process does not contain any reference to human embryos” (emphasis added).
Q1: What is meant by “human embryo” in the context of the Biotech Directive?

- “…any human ovum must, as soon as fertilised, be regarded as a “human embryo” within…Article 6(2)(c) [Biotech Directive], since that fertilisation is such as to commence the process of development of a human being”. Definition also includes
  - A non-fertilised human ovum into which the cell nucleus from a mature human cell has been transplanted
  - A non-fertilised human ovum whose division and further development have been stimulated by parthenogenesis
  - “as regards stem cells obtained from a human embryo at the blastocyst stage [i.e. usually pluripotent human embryonic stem cells], **it is for the referring court to ascertain, in the light of scientific developments, whether they are capable of commencing the process of development of a human being** and, therefore, included within the concept of “human embryo” within…Article 6(2)(c) [Biotech Directive]”
Q 2: What is meant by the use of human embryos for industrial or commercial purposes?

- Use of human embryos for scientific research which is the subject-matter of a patents cannot be distinguished from industrial & commercial use and cannot therefore avoid exclusion from patentability.

- Consequently, scientific research entailing the use of human embryos cannot access the protection of patent law.

- **Exception:** Patents on uses of human embryos are not prohibited under the Directive where they concern the use for therapeutic or diagnostic purposes which are applied to human embryo and which are useful to it –

  Ex.: correcting a malformation and improving chances of life.
Q 3: Patentability where patent (application) does not explicitly mention/claim using human embryos although they were required at some (earlier) stage?

“...an invention must be regarded as unpatentable, even if the claims of the patent do not concern the use of human embryos, where the implementation of the invention requires the destruction of human embryos. In that case too, the view must be taken that there is use of human embryos within the meaning of Article 6(2)(c) [Biotech Directive]. The fact that destruction may occur at a stage long before the implementation of the invention, as in the case of the production of embryonic stem cells from a lineage of stem cells the mere production of which implied the destruction of human embryos is, in that regard, irrelevant” (emphasis added)

FULL HISTORY APPROACH
Basic implications of the CJEU judgment

• CJEU follows the ethical approach taken by AG Bot but in clarifying the principles the Court appears to have further heightened morality threshold

• Pluripotent human embryonic stem cells may be “human embryos” and therefore unpatentable. The test to be applied by national courts being whether or not, in the light of scientific developments, they are “capable of commencing the process of development of a human being”.

• **Full history approach:** destruction of human embryos to create cell lines prior to the filing date of a patent is sufficient to bar patentability
Mixed reactions

- **Applause:**

- **Optimists:**
  Ewen Callaway, *European ban on stem-cell patents has a silver lining*, Nature 478, 441 (2011)

- **Harsh criticism:**

- **Violation of Art 27 (2) TRIPS? Further effect of full history approach?**
What about EPO?

The CJEU considered this to be the "same conclusion" as the EPO reached in Case G02/06. **Is this really so?**
Earlier EPO – decision concerning patentability of hESCs: Edinburgh Patent (EP 0 695 351)

- Method for modifying animal stem cells resulting in improved survival, facilitating selection, isolation and genetically modified cells for use in such methods.

- Animal/human

- Many years of proceedings with multiple opponents,

- Patent found to fall under EPC 53(a) and R 28(c) – uses of embryos in industrial or commercial purposes exempted from patent-protection

- Maintained in amended form in 2002
The EPO’s EBoA in G02/06 WARF (Nov. 2008)

• “WARF”: Application related to a patent application by Wisconsin Alumni Research Foundation

• Claims covered cell cultures comprising purified primate embryonic stem cells that can be prevented from differentiating by particular culturing.

• methods of obtaining cells not claimed

• WARF argued that hESC cultures not themselves “embryos” and no European consensus on morality issues surrounding hESCs

• Application was rejected by examiner: Art 53(a) and R28 (c) apply to the whole invention not merely the claimed subject matter

• Several questions were referred to the Enlarged Board of Appeals
R. 28 (c) forbids patent claims directed to human ESC cultures which at the filing date could be prepared solely by a method resulting in destruction of embryo.

Wording of claims not relevant but exploitation of invention.

Applicability of R.28 (c) must be assessed on date of application - that later scientific developments could avoid the destruction of the embryo was not significant.

Unnecessary to consider whether a consensus on ethics of hESCs in view of Biotech Directive.
EPO’s post WARF practice

• To circumvent the Rule 28(c) EPC exclusion from patentability patentees filed claims to inventions that could be reproduced using:
  - pluripotent human embryonic stem cells;
  - which could be obtained at the filing date from publicly-available cell lines

• EPO, as well as national patent offices (e.g. UKIPO) began to accept such applications, that did not directly involve destruction of embryos.

• More particularly: EPO established that human embryonic stem cell lines were readily available at least by May 2003; and generally considered patent applications based on such material and filed after this date not to be immoral (cf. eg EP application 05740642.3):
- **EPO’s post WARF practice appeared to imply that:**
  - pluripotent human embryonic stem cells are not “human embryos”
  - destruction of human embryos to create cell lines prior to the filing date of a patent is not sufficient to bar patentability of later inventions

- **EPO not bound by CJEU but there appeared to be a conflict with the CJEU’s “full history” approach**
  (although post WARF EPO not directly addressed by AG & CJEU)

- **CJEU also leaves open possibility for national courts to decide that pluripotent stem cells are considered to be “human embryos”**

- **However: Indications shortly after CJEU judgment that EPO intends to follow Brüstle and implement new principles in new Examination Guidelines (June 2012).**
Part G, Chapter II-17 to 18 on R 28 (c) (including bold text):

“(iii) Uses of human embryos for industrial or commercial purposes

A claim directed to a product, which at the filing date of the application could be exclusively obtained by a method which necessarily involved the destruction of human embryos from which the said product is derived is excluded from patentability under Rule 28(c), even if said method is not part of the claim (see G 2/06). The point in time at which such destruction takes place is irrelevant.

When examining subject-matter relating to human embryonic stem cells under Art. 53(a) and Rule 28(c), the following has to be taken into account:

(a) the entire teaching of the application, not only the claim category and wording, and
(b) the relevant disclosure in the description in order to establish whether products such as stem cell cultures are obtained exclusively by the use, involving the destruction, of a human embryo or not. For this purpose, the disclosure of the description has to be considered in view of the state of the art at the date of filing.

The exclusion of the uses of human embryos for industrial or commercial purposes does not affect inventions for therapeutic or diagnostic purposes which are applied to the human embryo and are useful to it (EU Dir. 98/44/EC, rec. 42).”
The EPO’s new examination guidelines II (Nov. 2014)

- Guidelines broadly reflect Brüstle ruling.

- Yet, somewhat clumsy wording "product, which at the filing date of the application could be exclusively obtained by a method which necessarily involved the destruction of human embryos from which the said product is derived is excluded" appears to be designed to allow for stems cell inventions related to cells produced by processes that do not necessarily require the destruction of an embryo, although it raises a number of questions.

- The stipulation that the inventions must not have required the destruction of an embryo at any time in the past is clearer.

  → invention many not employ stem cell lines that required destruction of an embryo at any point in history, although working the invention itself requires no such destruction (and regardless of whether or not such method is part of the claim).

- **Principles applied in T2221/10 Technion (February 2014)**
So what about the German BGH?
• Court (BGH) had to apply this ruling of the CJEU to its Brüstle case.

• reversed the judgment of the Fed. Pat. Court (PatG) and maintained patent with the proviso that hESC are not obtained by destruction of human embryos.

• clarifies that patent is maintained insofar as the human stem cells are obtained by other methods.

• BGH decision more permissive than PatG decision as it now encompasses human embryonic stem cells obtained by methods which do not lead to the (entire) destruction of the human embryo.

• Arguments:

  - patent-in-suit contains broad definition of SCs including embryonic germ cells, the production of which does not rely on the destruction of embryos.

  - Even at the filing date, the patent-in-suit could be worked without (entire) destruction of human embryos. (was that really so?)
Arguments (cont.)

- After filing date of the patent-in-suit, methods for the production of hES cells became available that do not require (entire) destruction of human embryos.

- methods include the generation of hES cells from so-called arrested embryos which, due to genetic defects, are impaired in their capacity to divide.

- Further, methods have been developed where only a few cells are removed from the blastocyst stage of the human embryo without affecting the capacity of the remaining blastocyst cells to develop into a living organism.

Conclusions

- BGH clarifies that stem-cell related inventions based on non-destructive methods are not excluded from patentability

- this provides perspectives for applicants in this field.

- **Note:** CJEU & BGH decisions do not question patent-eligibility of induced SCs, *i.e.* pluripotent cells derived from human reprogrammed adult cells.
“[T]he Office practice will now recognise that where the implementation of an invention requires the use of cells that originate from a process which requires the destruction of a human embryo, the invention is not patentable according to paragraph 3(d) of Schedule A2 [corresponding to Article 6(2)(c) of the Directive]. For example, where the implementation of the invention requires the use of a human embryonic stem cell line the establishment of which originally required the destruction of a human embryo, the invention is not patentable.”
Unsolved questions troubling courts in the UK!
CJEU distinguishing Brüstle: One of these things is not like the others ...

- Case C-364/13 International Stem Cell Corporation v Comptroller General of Patents

- Referring court: High Court Of Justice UK

- Question referred:

  Are unfertilised human ova whose division and further development have been stimulated by parthenogenesis, and which, in contrast to fertilised ova, contain only pluripotent cells and are incapable of developing into human beings included in the term "human embryos" in Article 6(2)(c) of Directive 98/44/EC on the Legal Protection of Biotechnological Inventions?

- Opinion of Advocate General, delivered on 17 July 2014:

  “A thorough analysis of the logic underlying the Court’s answer in Brüstle will lead me to propose an ‘exclusive’ answer to the question referred to the Court, i.e. excluding unfertilised human ova whose division and further development have been stimulated by parthenogenesis from the notion of ‘human embryos’ in light of the further specifications made by the referring court.”
“Article 6(2)(c) of Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions must be interpreted as meaning that an unfertilised human ovum whose division and further development have been stimulated by parthenogenensis does not constitute a ‘human embryo’, within the meaning of that provision, if, in the light of current scientific knowledge, it does not, in itself, have the inherent capacity of developing into a human being, this being a matter for the national court to determine.”
Summary: Patentability of Pluripotent Stem Cells

- **G2/06 WARF/Stem Cells** - an invention which necessarily involved the destruction of human embryos at filling date cannot be the object of a patent.

- **ECJ C-34/10 Oliver Brüstle v Greenpeace e.V.**
  - Any human ovum after fertilisation, any non-fertilised human ovum into which the cell nucleus from a mature human cell has been transplanted, and any non-fertilised human ovum whose division and further development have been stimulated by parthenogenesis constitute a ‘human embryo’;

- It is for the referring court to ascertain whether a stem cell obtained from a human embryo at the blastocyst stage constitutes a ‘human embryo’.

- Article 6(2)(c) excludes an invention from patentability where the technical teaching which is the subject-matter of the patent application requires the prior destruction of human embryos or their use as base material, whatever the stage at which that takes place and even if the description of the technical teaching claimed does not refer to the use of human embryos.

- Brüstle distinguished by national decisions (BGH) and the CJEU in ISCC
Conclusions & open questions I

- CJEU decision in *Brüstle* and *ISCO* binding on EU’s national courts

- CJEU concluded that “same conclusion” was reached as EPO in WARF, but “full history”- approach appears to contradict post WARF EPO practice

- EPO is formally not obliged to comply but has now decided to follow it.

- Yet, much will depend on the specific interpretations given to Brüstle by national courts and the EPO.

- Read new EPO guidelines and BGH Judgment which provide some leeway for potential patentees.

- Yet: A strict interpretation of Brüstle potentially still allows to preclude many patents on human embryonic stem cells per se, i.e. regardless of
  - whether derived directly from embryos or from previously established cell lines
  - whether totipotent or pluripotent,
Conclusions & open questions II

- Potential shift of patent activity to adult stem cells and induced pluripotent stem cells (in how far are hESC needed for this?)

- More focus on other aspects of stem cell therapy (treatment regime/culture media/delivery methods etc.)

- More (indirect) governmental involvement in hESC related R&D?

- More industry focus on US/int. patents, trade secrets, data exclusivity?

- CJEU judgments results in temporary uncertainty for industry: Older patents will remain valid until challenged in national Courts

- What about new techniques allowing for blastomere separation without destroying the embryo???

- BGH would allow these and the CJEU has now also distinguished Brüstle in ISCO.
Conclusions & open questions III

- A broader impact of full history approach on other technologies?

- Impact on investment / research in regenerative technologies in Europe/brain drain?

- Or more publicly financed research in the EU without risk of infringement?

- Should morality really be addressed in patent law, such as EPC & Biotech Directive? (intention: protecting biotech inventions & promoting investment in Europe, negative exclusionary right)

- **Paradox: Funding & Embryos that are discarded during in vitro fertilization would also fall under CJEU definition of Embryo**

- CJEU has formally last word on interpretation of the Biotech Directive, **but:**
Conclusions and open questions IV

- Competence of CJEU to decide on the definition of the embryo? Conflict with ECHR: Evans v. UK? Accession of EU to ECHR? CJEU/ECHR relationship?

- History of the legislative process leading to Biotech Directive fully recognized???

- Respect for different national and international definitions? Is their a democratic basis?

- Did the Court sufficiently consider the highly developed regulatory regime and ethical standards pertaining to hESC-research?

- What will happen in the unitary patent system?

- Violation of Art. 27 (2) TRIPS?

- Religious groups will stick to their own logics/values – will not be easily convinced by scientific arguments pertaining to definition of embryo
Moral Dilemma & Risk for over-simplification

- Not necessarily an old man
- Might be a severely suffering baby or child

-Might have been discarded: IV-fertilization-paradox?
-Might be considered to be merely an early stage association of high-potential cells without any nerves/human properties
-Destruction could sometimes be avoided, or
-occurred long ago but not when cells were actually isolated from a cell line
Readings for next lecture

1. Thursday, 26 Feb.: Patent Issues in Personalized Medicine (NR)

Required reading:
- The European Patent Convention Articles 52-54 (ABSALON)
- Examination Guidelines, Section G-VI, 7.1 (ABSALON)

Supplementary reading:
- Timo Minssen and David Nilsson, *The US Supreme Court in Mayo v Prometheus – taking the fire from or to biotechnology and personalized medicine?*, Queen Mary Journal of Intellectual Property, Vol. 2 No. 4, pp. 376–388 (ABSALON)

Preparation for the presenting group:
- **GROUP 4:** EPO’s Enlarged Board of Appeal (EBA) in G 2/08, ABBOTT RESPIRATORY/Dosage regime, 19 February 2010 (ABSALON).
Any questions or comments?

Further reading:

EU Pharma Law, IPR & Life Science:

Syllabus:

Supplementary info:
http://jura.ku.dk/pdf/uddannelsessesservice/european-pharmaceutical-law/

CSU Summer Course – Pharma Law & Policy for Professionals:

http://copenhagensummeruniversity.ku.dk/en/courses/pharmalawpolicy/

Harvard Blog:

http://blogs.law.harvard.edu/billofhealth/category/contributors/timo-minssen/
Faculty of Law
Additional slides
Brüstle v. Greenpeace in light of the forthcoming Unitary Patent System
Impact on patent practice

• Take aways for applicants, patent holders & patent practitioners
  – Prosecution
  – Litigation