



Ethical aspects of commercialization and patentability of stem cells and stem cell lines

*A workshop organised by EuroStemCell,
an EU Framework VI Integrated Project*

GRAND Hotel, Bantorget 1, Lund, Sweden
13-14 March 2006

INTRODUCTION

Can Europe afford to have different ethical standards than the US and Asia with regard to commercialisation and patenting of the products of stem cell research? What are the implications for European competitiveness?

These questions are explored in *Ethical Aspects of Commercialization and Patentability of Stem Cells and Stem Cell Lines*, the second in a series of EuroStemCell workshops that examine and discuss the ethical and societal issues relating to stem cell research.

WORKSHOP THEMES

Commercialization

- The chain of discovery –invention – design trial outcome – safety programme – production – marketing – distribution, and the stakeholders’ perspectives on the present situation, goals and obstacles.
- Ethical aspects concerning commercialisation of the human body
- Legal background
- Procedures and practices - the state of the art, problems and possibilities in different countries

Ethical aspects of patentability of human stem cells and stem cell lines

- Legal problems raised by patents on human stem cells: international perspectives
- Praxis of EPO and national patent offices
- Public Perceptions of ES and “life” patents
- Ethical problems raised by patents on human stem cells (methods and products)
- A glance at the future
- Patient Organization Perspectives

COUNTRIES REPRESENTED

Belgium
Canada
Czech Republic
Denmark
Germany
Great Britain
Italy
Portugal
Sweden

PARTICIPANTS

50 participants attended this workshop. Like the invited speakers, they represented the spectrum of communities interested in or concerned by the decisions made in the area of patenting and commercialization in stem cell research. Participants included scientists working in the area of stem cell research, lawyers, ethicists, philosophers, as well as the representatives of the European Patent Office, the EMEA and patients' organizations.

PROGRAMME

Monday March 13

Session I: Commercialization

- 13.00–13.15 Welcome and introduction
Göran Hermerén, Lund University, Sweden
Austin Smith, Institute for Stem Cell Research, University of Edinburgh
- 13.15–14.30 Panel 1: Stakeholder perspectives on present situation, goals and obstacles
Olle Lindvall, Lund
Rui Reis, Braga
Tim Allsopp, Edinburgh
Paul Torremans, Nottingham
- 14.30–14.55 Ethical aspects of “commercialisation” of the human body
Ludger Honnefelder, IWE, Bonn
- 14.55–15.30 *Coffee*
- 15.30–16.35 Panel 2: Interpretation and implementation of relevant laws and directives
Marisa Papaluca-Amati, EMEA, London
Aurora Plomer, Nottingham, UK
Lincoln Tsang, London, UK
- 16.35–17.35 Panel 3: Procedures and practices in different countries.

Josef Kure, Czech Republic
Anne McLaren, UK

17.35–18.30 General discussion

Tuesday March 14

Session II: Patentability of human stem cells and stem cell lines

08.30–08.55 Legal problems raised by patents on human stem cells: international perspectives
Geertrui van Overwalle, Leuven, Belgium

08.55–09.20 Praxis of EPO and national patent offices
Ingwer Koch, EPO, Munich

09.20–09.45 Public Perceptions of ES and “life” patents
Timothy Caulfield, University of Alberta, Canada

09.45–10.10 Ethical problems raised by patents on human stem cells (methods and products)
Michael Rogers, Brussels

10.10–10.35 *Coffee*

10.35–11.35 Panel 3: A glance at the future
Aliko Nichogiannopoulou, EPO
Christof Friedrich, EPO
Graeme Laurie, Edinburgh
Anne McLaren, Cambridge

11.35–11.55 Patient Organization Perspectives
Susanna Lindvall, Stockholm

12.00–13.00 Concluding Discussion

13.00 *Lunch and departure*

SUMMARY OF PRESENTATIONS AND DISCUSSIONS

This summary has been prepared by Kristina Hug and approved by the individual speakers. Opinions expressed are those of the workshop participants, and not necessarily those of EuroStemCell.

MONDAY MARCH 13

SESSION 1: COMMERCIALIZATION

Panel 1: Stakeholder perspectives on present situation, goals and obstacles

Prof. Olle Lindvall, Wallenberg Neuroscience Center, Restorative Neurology, Lund University, Lund, Sweden

- Problems and possibilities from the clinician's point of view
- Three strategies to use stem cells in brain disease treatment.
- Important developments to make stem cells clinically useful for brain diseases.
- Types of stem cells that can be used to obtain specific type of functional neurons.
- The road-map to the clinic in the case of stroke.
- Economical aspects of the development of stem cell therapy for neurological disorders.
- Take-home message:
 - Stem cell therapy has great potential but clinical development will require major research efforts and probably take long time
 - Costs for development towards the clinic cannot be covered by traditional research grants-involvement of industry needed
 - Stem cells of human origin necessary for clinical application
 - Embryonic stem cells and stem cells from foetal brain are most promising for treatment of neurological disorders.

Rui Reis, Director of the 3B's Research Group – Biomaterials, Biodegradables and Biomimetics, University of Minho, Campus de Gualtar, Braga, Portugal

- What is involved in the creation of a new tissue/organ.
- The EU legislation on Human Tissue Products and possible regulatory gaps.
- The objectives of the EC regulation.
- Important issues regarding Advanced Therapies.
- The key features of the future regulation.

Tim Allsopp, Stem Cell Sciences Ltd., Edinburgh, UK

- Requirements of available and widespread, safe, effective stem cell therapies
- Converting the discovery to invention.
- Reducing invention to practice.
- Ownership of the cell lines.
- Important questions (especially acute for small organisations) that need to be answered:

- Who will own stem cell lines?
- Altruistic donation versus financial incentives?
- At what point a discovery in biotechnology is converted into an invention?
- Should the research sponsor be able to use and sell differentiated cells at cost of production only?
- What financial gain may be gained by the company?
- What is the place of ethical review?

Prof. Paul Torremans, School of Law, Nottingham, UK

- The way moral and ethical concerns are reflected in patent law clearly points in the direction of a distinction between what can be called (in a broad sense) the raw material that is donated in a non-commercial context and maybe the stem cells themselves on the one hand and the stem cell related inventions or applications that may follow from human intervention with the raw material. The exclusion of the whole chain cannot be justified.
- In the latter stages there is what could be described as a pure commodification of the human body. There is the added value of human intervention and there is I would suggest the potential beneficial effects of any treatment that may result from the use of human embryonic stem cells.
- There is a difficult question as to where one should draw the line between what can be allowed in terms of commercialisation open for further discussion. Morality and other concerns can also work outside patent law. The grant of a patent is by no means an authorisation to implement the invention, let alone a stamp of moral approval.

Ethical aspects: Commercialisation of the human body

Ludger Honnefelder, German Reference Centre for Ethics in the Life Sciences, Bonn, Germany

- Overview of the philosophical background relevant to stem cell research and the moral status of the human body, as well as the question of financial gain.
- Ethical Aspects: Commercialisation of the Human Body.
- Examples for the (potential) use of body parts in medicine and research.
- The new challenge: embryos and stem cells for research, and the number of ethical and legal problems related to this challenge.
- The Council of Europe prohibits financial gain from the human body. However, it is important to note that the explanatory memorandum to the Convention on human rights and biomedicine states that patents are not excluded.

Panel 2: Interpretation and implementation of relevant laws and directives

Marisa Papaluca-Amati, Deputy Head of Sector Safety and Efficacy, Pre-Authorisation evaluation unit, EMEA, London, UK

- EMEA'S role in human medicines field.
- A wide spectrum of complexity of medicinal products.
- **Advanced therapy products: Are they only medicinal products or something else at the same time?** When we are confronted with something made of cells, we often do not know if that counts as medicinal product or not. Or should it count as a potential medicinal product – that is, not transplantation and not medical device? Medicinal products may range from chemicals to manipulated cells. But overall the cell therapy products are a new area. When it comes to medicinal products, where the source is human material – we already have plasma, blood, etc, which were used as a source material. It is not completely new to use material of human origin. In the regulatory framework, cell therapy-based products could be fully classified as medicinal products, but the carriers can be classified as medical devices. There is also a heterogeneity on how cells are regulated depending on whether they are autologous and allogeneic products.

Aurora Plomer, Reader in Law and Bioethics, School of Law, University of Nottingham, Nottingham, UK

- The Construction of Moral Exclusions in the EU Directive on Biotechnological Inventions: Competing Interpretations
- Overview of the legal parameters, which create the framework within which the construction of the moral exemptions in the Directive has to take place.
- Moral Diversity & Need for Margin of appreciation: European Court of Justice
- Margin of Appreciation: European Court of Human Rights
- Article 2 of the European Convention of Human Rights (ECHR)
- European Convention on Human Rights & Biomedicine (CHRB): Article 18
- **Summary Conclusions**

- Moral exclusions on patents have to reflect the normative unity and legal integrity of EU and Human Rights law.
- Margin of appreciation is required in the interpretation and application of moral exemptions and principles in order to accommodate differences in legal and moral cultures.
- EPO's "broad approach" is not consistent with the legal parameters bounding the construction of Article 6.
- Procedural options: Introducing Patent Ethics Committees? Would that mean the duplication of work with Research Ethics Committees or conflict with Research Ethics Committees?
- Interaction between national and supranational ethics committees?
- Prior ethics approval before a patent is granted?
- Whatever interpretation one puts on Article 6 it has to fit the legal parameters set in the text of the Directive and identified below. The text of the directive does not envisage patent law to set moral norms independently of national and supranational laws but instead envisages the relevant applicable moral principles to be identified from and embedded in the national or international laws recognised in a member state.

Lincoln Tsang, Arnold & Porter LLP, London, UK

- **Stem Cell Regulation in the European Union.** The regulatory landscape in Europe is increasingly complex with regard to the regulatory control of cell-or-tissue based products. A cell-or-tissue based product is only regulated as such if it falls within the definition of a medicinal product as provided in Article 1(2) of Directive 2001/83, which has been recently revised by Directive 2004/24.
- A substance incorporated into a medicinal product may include any matter derived from human or animal sources therefore, human or animal stem cells that are administered to human subjects for the purpose of treating or preventing the disease through modifying physiological functions may be captured by the broad legal definition of a medicinal product.
- Currently the European Commission has proposed a new regulatory framework to capture cell-based products, which are used for regenerating, repairing or replacing a human tissue. The proposed regulatory framework is to extend the current regulatory regime for medicinal products to this new class of products under the broad therapeutic class of "advanced therapy medicinal products".
- The quality and safety of the source cells are regulated under Directive 2004/23 which sets out standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human cells and tissues for human application.

Panel 3: Procedures and practices in different countries.

Dr. Josef Kure, University Center for Bioethics, Masaryk University, Brno, Czech Republic

- Societal expectations and how biomedical research is perceived in Central and Eastern European Countries (The society in the Central and Eastern European countries is not a homogeneous society. Some countries show great expectations, whereas others do not).
- Human Embryonic Stem Cell Research: Central and Eastern European Cultural Context (Central and Eastern European countries had a common destiny during 1945 – 1989, but there is much difference among them in terms of religion and culture).
- The way towards the Bill on human embryonic stem cell research in the Czech Republic. Commercialization and Patenting (limited to the Czech Republic)
- Policy typology on human embryonic stem cell research in the Eastern Europe

Restrictive	Unclear	Permissive
Poland	Latvia	Czech Republic
Slovakia	Bulgaria	Hungary
Slovenia	Romania	Estonia
Lithuania	Croatia	

Prof. Anne McLaren, The Wellcome Trust/Cancer Research UK Gurdon Institute, University of Cambridge, UK

- Self-renewing embryonic stem cell lines are not body parts, but artefacts of culture system
- It would be ethically desirable that stem cell lines from stem cell banks should be provided free of charge. The bank may ask for payment for stem cell lines if they are going to be used for toxicity testing, or in other ways that would contribute to profits. Stem cell lines could also be exchanged. But if they are to be used for industry – then a charge would be expected.
- The issue of payment to donors is an interesting one. There may be particular donors who may be able to provide particular embryos that would be extremely valuable for a stem cell bank. Should they not be induced to donate by some payment?
- The situation will change, when stem cells become used for clinical treatment. It will depend if they are to be used in publicly- or privately-funded health services, or industry-funded trials. My conclusion is that at least in the UK there is no absolute bar for charging if stem cell lines are to be used for profit.

GENERAL DISCUSSION

- **Harmonisation of rules is desirable for many good reasons**, but it may be very difficult to achieve, having seen all the religious and cultural differences in Europe. Very different rules in different countries would create difficulties. It is important to have joint recommendations, and the future rules should not create diversity. The first priority should not be to have the same regulation in all countries, but rather **to address the rules, which create more problems first**.
- We should make a **clear distinction between prohibition of commercialisation of the human body as such and commercialisation of products or ideas**, which patenting is

all about. The law-makers might not know or make that distinction. The danger is that this **might lead to total ban of commercialisation.**

- There is no general answer when something becomes a product and ceases to be a body part: **we must look at specific areas.**
- The **Oviedo Convention** has been written in the Christian tradition in the fear of organ trafficking. But it **does not exclude patenting and compensation for damage.** Removed parts cannot be used for other purposes than the declared ones. In the context of biobanks, this requirement creates difficulties - how to deal with informed consent?
- From the point of view of health economics, **what would be the cost for taking cell-based therapy to the clinic?** Pharmaceutical companies must have tried to do these sums. What they spend on animals using them for testing for toxicity, and how much they would spend if they used stem cell lines instead.
- We should **keep ethical issues out from the patenting process.** Patent engineers have no training in ethical review, so it should be done by someone, who is used to do this kind of evaluation. The Patent Office should not straightforwardly discuss ethical matters, but it should pass the problem to a group of ethicists and they would solve it. It is required **to devise a new ethical evaluation procedure.**
- It may happen that in some years the invention, the patent application of which has been rejected, may be considered in consensus with the respect to ethics, but the applicant has lost on his invention, because he was a few years too early. **If we had two evaluation systems, technical and ethical,** the applicant could pass the technical system and wait until the ethical agreement is achieved, and then get the patent.
- It would not be necessary to deal with ethical issues in patenting, if morality and *ordre public* was an evident concept and agreed upon by all member states. The emergency solution could be to introduce some major ethical points into patent law. Now we apply the patenting in areas, which has never been the patenting subject before. The question is, **how this instrument (patenting), that has its origins in very different technical areas, can now be applied in the new areas of biotechnology.**
- When drafting the EU Biotechnology Directive and putting the ethics into the patenting system, the legislator had in mind the protection against pornography, letter bombs, etc. Can inventions stemming from the embryonic stem cell research be viewed in the same light?
- **If you want industry to invest in developing products for the treatment of rare diseases, economical revenue to the industry cannot be banned.** The first therapies, if and when they are available will be very expensive. The question of access will become important. If the aim of such therapies is public health, what is to be said about the 3rd world, especially about rare diseases there?

TUESDAY MARCH 14

SESSION II: ETHICAL ASPECTS OF PATENTABILITY OF HUMAN STEM CELLS AND STEM CELL LINES: PROBLEMS AND POSSIBILITIES

Legal problems raised by patents on human stem cells: international perspectives

Prof. Geertrui van Overwalle, Centre for Intellectual Property Rights, Law Faculty, Catholic University Leuven, Leuven, Belgium

Players

- In patent granting activity in the field of stem cells the major active players are the United States, Japan, Australia, Great Britain, China and the EU. The presentation focuses on (1) the legal framework and granting practice of (2) human embryonic stem cells in (3) Asia, Australia and the US. Special attention is paid to the morality clause and the list of excluded subject matter. As a standard of reference, the morality clause and the list of excluded subject matter in Europe are first presented.

Legal Framework

- **Morality clause is omnipresent.** Asia is no longer an “underdeveloped” IP region.
- **Although the morality clause is omnipresent, its scope and interpretation is differing.** For example, it includes “public order” in Japan, Taiwan, Korea, which also leaves a narrow gate of entry. It includes “public policy” in the US, “public interest” in China, “well being of the society” in the US, “public health” in China, Japan, Taiwan and Korea, “morality” in Japan, Taiwan, Korea and the US, “social morality” in China, “offensive, immoral or anti-social behaviour” in Singapore and “law” in Australia (the latter leaving a wide gate of entry).
- The **list of exclusions** also differs greatly and is rather exceptional (not omnipresent). It includes “cloning human beings” in China, “biological processes for generation human beings” in Australia, “cloned human beings” in China, “human beings” in Australia, “human embryos in the US, “use of embryos” in China, “human/nonhuman chimeric embryos” in the US.
- **Industry’s point of view** is well reflected in an AIPPI Resolution:
 - **Resolution Q 114 (Executive Committee Berlin, September 2005)**

- Patents should be available without any discrimination for all kinds of inventions, including biotechnology; the prevention by countries of the exploitation or use of certain technologies should not exclude those technologies from being patented;
 - Inventions based on isolated human embryonic stem cells should be treated like any other invention and should be patentable if the general patent criteria (novelty, obviousness/inventiveness, industrial applicability and sufficiency of disclosure) are met;
 - Exclusions to patentability due to the principles of *ordre public* and morality may be applicable but should be as limited as possible and should be defined precisely.
- **Patent practice and case law.** Many patents have been filed, many are still pending, few have been granted.

Routes for reflection.

- **There is a danger of “backward looking”** – looking at the prehistory and where the stem cells came from. In the international perspective, we may also have definition problems, as the concept of “human embryo” differ from country to country. There are different views in current national legislations on what is considered as “human being”. There is also lack of consensus whether the term “embryos” means spare embryos or created embryos. There is also discontinuity in research regulation/patent legislation.
- Regarding the morality clause, it is important not to fall into the so-called “**morality trap**”: A wrong question to ask is: Is research/invention contrary to *ordre public* and morality? The right question: Is commercial exploitation of research results contrary to *ordre public* and morality? Is giving a patent monopoly for research results/invention contrary to *ordre public* and morality?
- Do we have the “**tragedy of the ethics**”? The importance of ethics might have negative impact on European competitiveness.

Praxis of the European Patent Office and national patent offices

Dr. Aliko Nichogiannopoulou, European Patent Office, Munich, Germany

- Praxis of the European Patent Office (EPO) and National Patent Offices
- Main patentability requirements
- Additional patentability requirements
- Article 53(a) of the European Patent Convention (EPC)
- “*Ordre public*” & Morality:
 - “*Ordre public*”;
 - Protection of public security;
 - Protection of physical integrity of individuals;
 - Protection of the environment.
 - Morality
- Morality is related to the totality of accepted norms of right and wrong in a particular culture. For the purposes of the EPC, the culture in question is the one inherent in

European society and civilization. Case Law: “Conventionally accepted standards of conduct of European culture” (T 356/93)

- It is difficult to define “ordre public”, “morality” and “European culture”. Europe is a small continent but very multicultural. It can be said that for a patent examiner to define “European culture” is a task impossible to perform – as well as to define what is right or wrong. The **patent examiner is not qualified to do this kind of work**. Situation was bad enough before the EC Directive on legal protection of biotechnological inventions was enforced, but now there is no end to despair either, since it is unclear how to interpret the requirements for the Article 6. We need a consensus among the member states to have judgements to establish what is in the “European culture”.
- There is also a lack of consensus among the ethics committees about what is patentable. In my opinion, embryonic stem cells are an artefact, since they do not exist in nature. Foetal and adult stem cells exist in *in vivo* populations and can thus be described as isolated body parts. Embryonic stem cells (as pointed out by Anne McLaren) are NOT body parts.
- There have been only four patent applications dealing with human embryonic stem cells that have passed the first instance of the European Patent Office's examination procedure.
- **Boards of Appeal at the EPO:**
 - **Technical Boards:** The **Technical Boards of Appeal** give independent final rulings on appeals against decisions taken during grant and opposition proceedings.
 - **Enlarged Board:** The **Enlarged Board of Appeal** gives decisions and opinions in order to ensure correct application of the law, or if an important point of law arises.
- People who have strong opinions on the patentability issue in a certain case may send “amicus curiae” letters to Board.

Public Perceptions of ES and “life” patents

*Prof. Timothy Caulfield, Faculty of Law, University of Alberta, Edmonton, Alberta, Canada
(Also: Canada Research Chair in Health Law and Policy, Health Law Institute, University of Alberta, Edmonton, Alberta, Canada)*

- Are the emerging issues eroding **public trust of biomedical research**? This may especially be true regarding the socially contentious issues, like commodification of human biological material. In focus groups, the more people learn, the more hesitant they become about some kinds of biotech patents. For some, the idea of patenting a life form involved the commodification of life and was hence seen as morally wrong.
- **Patents and Access.** More people are “uncomfortable with the idea of providing patents in the area of biotechnology” because it will adversely impact access to useful technologies (49%) than felt that “patent protection is necessary in the field of

biotechnology because we need to encourage inventions in this area for all the benefits they can bring” (33%). (Pollara/Earnscliffe, 2002)

- **Access and Biotech** (Einsiedel, 2005)
 - There is general support of the public for rewarding innovation;
 - Support declines regarding “life patents”;
 - “There is something wrong with the idea of patenting parts of a life form such as an animal or plant” (50 % Canada, 45 % U.S.) (BACC, 2003);
 - The public is more likely to accept if they see potential benefits, E.g., health care vs. agricultural research;
 - There are concerns regarding the commodification: the idea of patenting a life form involved the commodification of life and was hence seen as morally wrong (Industry Canada, 2003);
 - There is concern about impact on access;
 - There is strong support for a consideration of ethical issues.

- **Regarding Stem cell Patents:** “Both supporters and opponents of stem cell research and therapy may find many of these commercial developments to be morally disturbing.” (Resnik, 2002)

- **Commercial Involvement.** “Most people rest their assessment of credibility on the degree to which the person or institution is perceived to be at arm’s length and independent of controlling and/or funding influencers. The source of the funding seems to be the critical test.” (Pollara & Earnscliffe, 2000)

- **Independent governance scheme** may be created for large, publicly funded, research initiatives. It should have clear, transparent mandate (e.g., research in the public interest, commercialization strategies that allow reasonable access to technologies and research tools). Such a scheme would create distance between IP decisions and researchers, and would be formulated with input from public.

- **IG (independent governance) and PP (patent pools): Will it help? These schemes face the following challenges:**
 - Pre-innovation needs to be done
 - Will researchers sign up?
 - Negotiating with funding agencies, universities and industry
 - Meaningful public engagement
 - Difficult to manage on an international scale (which is key)

Ethical problems raised by patents on human stem cells (methods and products)

Michael Rogers, Group of Policy Advisors, European Commission, Brussels, Belgium

- **The governance of science advice - Some important messages:**
 - Transparency in the selection and use of expertise is essential.
 - Broadening the expertise base in policy advice is necessary.
 - Integrating expertise in all stages of risk governance is important.
 - Expertise is increasingly sought but increasingly contested.
- **The European Group on Ethics in Science and New Technologies (2005-2009) demonstrates the principles of: quality, openness and effectiveness.** The Group is an independent, pluralist and multidisciplinary body, which advises the European Commission on ethical aspects of science and new technologies.
- Opinions are Provided:
 - At the request of the Commission, or
 - On the EGE's own initiative or
 - The Parliament and the Council drawing the Commission's attention to particular issues
- **Development, adoption and publication of the Opinions**
- **Opinion Number 16: Patenting and Human Stem Cells**
- Produced following a formal request of the European Commission dated 18.10.2000.
- **EuroStemCell Mission: To take stem cell technology to the clinic.** This requires Freedom of Research and Investment. The Mission of the EuroStemCell is highly relevant to Opinion 16.
- **We should strike the balance** between freedom of research and the protection of investment, and between the encouragement of progress and the provision of access to health care.
- **The EGE Opinion:**
- New knowledge is essential for the development of individuals and societies (20 – 6.3.2). However, it **must be restricted by respect for other important values and ethical principles** (20 – 6.3.2). We should **avoid patents that are too broad** that would impair further research and development (16 – 2.7).
- **Patents Can:**
 - Encourage Scientific Progress and hence Better Health Care (16 – 2.2), but,
 - Limit Access to Health Care Products due to License Fees (20 – 6.3.2).
- **Directive 98/44: What is “In”?**
 - 3.1 “Inventions that are **new**, involve an **inventive step**, and are **capable of industrial application**, - “**even if**” biological in nature”

- 3.2 “Biological material isolated from its natural environment or produced by a technical process “**even if**” previously occurring in nature”.
- **Directive 98/44: What is “Out”?**
 - 6.1 “Where commercial exploitation is contrary to ordre public or morality”.
 - 5.1 “Simple discovery of one of the elements of the human body (including gene sequences)”.
 - 6.2 “a) cloning of human beings, b) modifying germ lines of human beings, c) **uses of human embryos for industrial purposes**”
- **Directive 98/44: Recital 20 (patentability)**
 - “... an invention based on an element isolated from the human body or otherwise produced by means of a technical process, which is susceptible of industrial application, **is not excluded from patentability**, even where the structure of that element is identical to that of a natural element, given that the rights conferred by the patent do not extend to the human body and its elements in their natural environment”.
- **Source of Biological Material in the EGE Opinion:** Donors should be given clear information regarding the conditions under which the donated tissue will be used and on the likely public health benefits. Information should include the foreseeable use of the tissues.
- **Elements Isolated from the Human Body can be Patented (Cf. Recital 20 above).** The element would still have to meet the standard criteria for patentability – in particular the inventive nature and industrial applicability.
- **EGE 16 – 2.3** comes to the same conclusions as those presented in Directive 98/44 but emphasises “specific use” rather than “industrial application” in order to avoid “too broad patents”.

Panel 3: A glance at the future

Dr. Aiki Nichogiannopoulou, European Patent Office, Munich, Germany

- If the European Patent Office (EPO) takes a more restrictive approach, this is not because the EPO wants to hinder research advancement, but because the EPO is subject to pressures from many sides.
- Regarding the patentability of stem cells, can there be technical solutions to a moral dilemma?
 - E.g. parthenogenetically derived blastocysts, which can never give rise to an organism. Parthenotes are not viable. Can inventions based on them be patentable?

- E.g. Blastocysts derived from dispersive embryos. A triploid embryo would also not be viable. It is considered as discarded material. If such embryos were taken “from the trash”, and converted into diploid embryos – could the research be conducted on them?
- E.g. altered cell nuclear transfer, when a nonviable zygote is created. If such zygotes are used for research, there is no destruction of any viable human embryos, so it may seem that research on such zygotes cannot be unacceptable.
- It can be argued that such discarded material is not completely “trash”, since it can be saved, and thus research on such material is not ethically unquestionable.
- Would these arguments mean that as long as scientists manage to create human embryos that are not viable, they would get a green light for conducting research on them?

Dr. Christof Friedrich, European Patent Office, Munich, Germany

- It is currently under dispute how broadly Rule 23d(c) of the European Patent Convention (EPC) should be interpreted. In case of a broad interpretation, subject-matter derivable from **and only from** human embryos would not be patentable.
- It is, in this case, not relevant how distal in terms of production steps the subject-matter is. It rather matters whether following back the chain of production one **necessarily and inevitably** arrives at the use of human embryos.
- This was the approach taken by the Examining Divisions in recent cases at the EPO. In case of a narrow interpretation, and this is the position most applicants and patent proprietors take, it only matters whether claimed subject-matter falls within what is exempt from patentability. The "history" of production should not matter when assessing patentability under Rule 23d(c).

Dr. Graeme Laurie, School of Law, University of Edinburgh, Edinburgh, UK

- There are many ethical issues relating to biotechnology and many of these become conflated and confused in the context of the role of the patent system. In Europe we expect too much of the morality provisions in patent law. **We overlook other areas of patent law, which can also address ethical concerns, for example, we could have better use of research exemptions or compulsory licences.**
- **The key issue is to ask the right ethical questions of the patent system and not to focus too much on the morality clause**, since there can be mixed messages about the true concerns. Are we concerned about the morality of the science or of monopolies over the science? It should be the latter.
- In this context, the focus on morality concerns should be a narrower one. We should consider the appropriateness of granting a monopoly over a certain invention, not the

morality of the invention itself. In other words, **we should ask whether commercialisation is problematic - this is a proper focus of morality in this context.**

- A failure to draw this distinction will create a blurring of the respective roles of the patent system and the regulatory system, and this is to be avoided. We need more work on the relationship between the two systems and their effects on each other.
- Being concerned about the morality of monopolies might mean, for example, that we conclude in some cases that the value of an invention is so great for society that we should not allow a monopoly over it; but this requires a prospective consideration of the use of the monopoly which would be very difficult to determine.
- Alternatively, we might consider retrospective concerns and deny patent protection because regulatory requirements have not been respected, for example, obtaining appropriate consent from research participants. Most importantly, however, **the patent system should not come to usurp the regulatory system.**
- Regarding benefit-sharing in stem cell research, there are community benefits which go beyond health benefits. Recent public engagement work indicates that **public may be less accepting of life science research if excessive profits are seen to be made through commercialisation.** Properly conceived benefit sharing models – to include some kind of distribution of wealth benefits to communities – could help to address such concerns.

Prof. Anne McLaren, The Wellcome Trust/Cancer Research UK Gurdon Institute, University of Cambridge, UK

- Human oocytes (or unfertilised eggs) are badly needed for clinical treatment for women who have no oocytes in their ovaries (e.g. 39X0 women), and also for those whose oocytes are no longer very good, e.g. women in their late forties when they have a low chance of success with IVF.
- Human oocytes are also needed for research, e.g. for somatic cell nuclear transfer (SCNT), for making stem cell lines. For analysing very rare genetic diseases, or diseases of very complex origin, stem cell lines from affected patients would be great research tools.
- Oocytes for research may be donated. In the USA it is OK to sell your oocytes for clinical treatment but not for research. **What is the ethical difference between the two?** In Israel, on the contrary, oocyte donation either altruistic or paid (either in cash or in kind) is against the law. Oocyte sharing is illegal in Singapore.
- **Are there other sources of oocytes?** Harvested **immature oocytes**, which are not good for clinical treatment, can be matured in culture and then used for research.

- Oocytes **from other species** might be used for research on SCNT. This raises a question: an oocyte from another species with a human nucleus – is that a human embryo or not?
- There are claims that **oocytes and sperm can be derived from mouse embryonic stem cell lines**. **If the same could be done from human embryonic stem cell lines** obtained using SCNT, problems of social ethics could arise.
- **If such oocytes were good, perhaps they could be patentable?** According to Article 5(2) of the EC Directive on legal protection of biotechnological inventions, **if oocytes produced in culture were indistinguishable from oocytes in the human body, would they not be patentable?**

Patient Organization Perspectives

Susanna Lindvall, Vice president of the Swedish Parkinson's Disease Association. Stockholm, Sweden

(Also: European Parkinsons' Disease Association) Stockholm, Sweden)

- Patients are suffering from incurable diseases, and their voice is an important reminder to the policy makers and legislators. **Patients organisations and their opinions must be taken into consideration when regulating stem cell research.**
- **Patients want** to live their life with dignity (they do not want longer life, but life with dignity);
 - They hope the results will benefit them;
 - They want cure or effective treatment;
 - They want to prevent their children and grandchildren from PD;
 - They want fast and safe results;
 - They also expect the researchers to join the debate!
- **Patients' opinion regarding stem cells**
 - They regard stem cell research as most potent possibility to deal with PD-caused problems;
 - They see stem-cell-based therapies as more “natural” when compared with drugs;
 - They expect less side-effects from stem-cell-based therapies;
 - Patients are willing to donate cells and tissues for research (if patients are asked to donate they are very willing to do that and want that material to be used in research. They do not feel being research persons for someone else);
 - They are willing to participate in research;
 - They expect stem-cell therapies to make normal life possible;
 - They think that research must advance fast – now!
- **Patients worry that:**
 - Clinical research is slow; it is slower than preclinical research;
 - Political decisions would make stem cell research more difficult;

- Economic restraints would not be favorable to stem cell research;
 - Promising researchers will emigrate to other countries because of better possibilities or better payment;
 - Commercialisation would inhibit research for rare diseases;
 - Patents would inhibit research (only some have these worries).
- **We should find a balance in commercialisation.** There should be **more government support for stem cell research.** Patentability should not prevent the accessibility of new therapies.
 - The question of informed consent must be well-regulated: donors must be asked for permission when using their blood, tissues, eggs, etc.
 - *What can we do together?*
 - Lobby;
 - Obtain and provide more information;
 - Encourage participation in the debate;
 - Support research;
 - Develop alliances;
 - Work together!

CONCLUDING DISCUSSION

Can Europe afford to have different ethical standards than the US and Asia with regard to commercialisation and patenting of the products of stem cell research? What are the implications for European competitiveness?

- **Distinction should be made between ethical and legal concerns.** They are different and a lot of confusion arises when the distinction is not clearly made. The challenge is to discuss ethical and legal issues separately. We should evaluate the consequences, but we should not mix oil and water.
- **Can we, Europeans, afford to have different standards to those they have in other countries** (e.g. Singapore, Japan, Korea, India, China, etc.)? It is important for our European competitiveness to be strong. Different ethical standards can create different policies and different research possibilities. There is a price to pay for having different standards (e.g. different standard of living, different standard of human dignity). Can we say “no” to everything and pay the price? But we cannot say “no” and pretend that no price will be paid. **It is wrong to misuse the precautionary principle**, which is also an ethical standard.
- There is a counter-argument to the assumption that higher ethical standards are lowering chances on the market. If we look at business ethics, their ethical codes of their own are increasing. **Trust and reputation is the basis of acceptability and acceptability is basis**

for success on the market. If we look at long-distance perspectives instead of short-distance perspectives, **in the long run it will pay off to have high ethical standards.**

- It would be the **responsibility of the governments not to allow too much financial interest in health care.** In the world we live today we have to work with industry, since governments will never pay and give all the funds necessary for stem cell research. In Europe we have a tragedy of investments disappearing: the governments do not invest in stem cell research. The unclear regulatory framework makes the banks, the investors to withdraw. If researchers have enough funding and continue the research, they may find promising results. It would be **beneficial for researchers not to be bound to a specific industrial sponsor.**
- **The non-treatment costs are very rarely measured.** What is often measured are the costs of adverse reactions. Stem cells may provide many scientific tools.
- Some people are uncomfortable about embryonic stem cell research, but there are not so many statements of being absolutely against. **It is normal that undecided people are uncomfortable. Therefore they should not be left alone only with the media.** The media is an important actor on the stage in that the media shapes the people's views by what they write and what they do not write. We should create a platform where patients' organisations, research organisations, industry and legislators would **work to decrease the uncomfortable status of public.**
- **Public-private partnerships are extremely valuable:** e.g. partnerships between pharmaceutical companies and medical research councils. In clinical trials, the advantage is that the pharmaceutical company invests money in a clinical trials, and **the public feels more comfortable when it is not just the pharmaceutical company that invests the money and when the funding is in cooperation with the research council.** The public has the right to feel more comfortable, as in this way (when it is also the research council which cofunds the research) there is **no fear that results unfavourable to the pharmaceutical company will not be published.**
- **Before the regulation is written, it is important to discuss what the ethical issues are.** It should be clearly decided what exactly is regulated, and what the ethical aspects of the regulated area are. Discussing the morality clause in patenting we should look at the context of morality provisions. **What is important is not to get a monopoly in a way you use and exploit your patent.** If we take into account morality clause it should be limited to commercialisation. **The morality clause has to be narrowed, otherwise it becomes a trap for many beneficial inventions.**
- There is a vacuum of ethical standards of behaviour in exercising patent rights. We should develop ethical standards in exercising patent rights.
- When discussing the ethical issues of patentability of stem cells, it is relevant to take into consideration the discussion on the patentability of genes. Genes are not stem cells and stem cells are not genes, but the discussion is relevant. In human stem cell patenting we are **still in the first discussion stage – discussion on existence, not on exercising of patent rights.**
- **Embryonic stem cell patents are an exception,** since the general trend is towards strong patent and protected patent rights.
- **The society feels uncomfortable about the proximity of industry interests.** But the benefit-sharing might help to reduce this feeling.

- The Directive tells that human body and human embryo are unpatentable. This provision was written by a legislator who is not a scientist. **If the legislator had explicitly said “germ cells”, how could we possibly include the embryo. The directive should be understood by ordinary people. Therefore it was written in the ordinary language** stating that human body does not include patentable inventions.
- Article 6 of the Directive on the protection of biotechnological inventions lists uses of embryo but not uses of human body as unpatentable inventions. However, **Article 6 cannot be treated as an exhaustive list.** If something is not mentioned there, it must have a meaning.
- Regarding benefit-sharing - it should be decided **who should get the benefits, what forms should those benefits take and how much should be given as well what the procedure of benefit-sharing should be.** If benefit-sharing is applied, the public should be able to view how these decisions are made.
- **The access and credibility of science is also a very important issue.** It is important to have regulatory mechanisms, indicating in what ways we would make the research benefits available to the community. **How much Europe would remain Europe if patients were deprived of possible therapies?**

APPENDIX 1: LIST OF THE SPEAKERS

- Tim Allsopp, Stem Cell Sciences Ltd, Edinburgh, UK
- Prof. Timothy Caulfield, Faculty of Law, University of Alberta, Edmonton, Alberta, Canada (Also: Canada Research Chair in Health Law and Policy, Health Law Institute, University of Alberta, Edmonton, Alberta, Canada)
- Dr. Christof Friedrich, European Patent Office, Munich, Germany
- Ludger Honnefelder, German Reference Centre for Ethics in the Life Sciences, Bonn, Germany
- Dr. Josef Kure, University Center for Bioethics, Masaryk University, Brno, Czech Republic
- Dr. Graeme Laurie, School of Law, University of Edinburgh, Edinburgh, UK
- Prof. Olle Lindvall, Wallenberg Neuroscience Center, Restorative Neurology, Lund University, Lund, Sweden
- Susanna Lindvall, Vice president of the Swedish Parkinson's Disease Association. Stockholm, Sweden (Also: European Parkinsons' Disease Association) Stockholm, Sweden)
- Prof. Anne McLaren, The Wellcome Trust/Cancer Research UK Gurdon Institute, University of Cambridge, UK
- Dr. Aliko Nichogiannopoulou, European Patent Office, Munich, Germany
- Prof. Geertrui van Overwalle, Centre for Intellectual Property Rights, Law Faculty, Catholic University Leuven, Leuven, Belgium
- Marisa Papaluca-Amati, Deputy Head of Sector Safety and Efficacy, Pre-Authorisation evaluation unit, EMEA, London, UK
- Aurora Plomer, Reader in Law and Bioethics, School of Law, University of Nottingham, Nottingham, UK
- Rui Reis, Director of the 3B's Research Group – Biomaterials, Biodegradables and Biomimetics, University of Minho, Campus de Gualtar, Braga, Portugal (Also: Department of Polymer Engineering, University of Minho, campus de Azurem, Guimaraes, Portugal).
- Michael Rogers, Group of Policy Advisors, European Commission, Brussels, Belgium
- Prof. Paul Torremans, School of Law, Nottingham, UK
- Lincoln Tsang, Arnold & Porter LLP, London, UK

APPENDIX 2: List of registrants

	Timothy	Allsopp	Stem Cell Sciences Ltd.,Edinburgh	UK
	Elin	Andersson		
	Magnus	Andersson	Committee for the patent protection of biotechnological inventions	
Prof	Anders	Björklund	Wallenberg Neuroscience Center, Lund University	Sweden
	Joeri	Borstlap	Charité Universitätsmedizin Berlin CellNet	Germany
	Susanne	Bremer	European Centre for the Validation of Alternative Methods, Institute for Health and Consumer protection	Italy
Prof	Timothy	Caulfield	Faculty of Law, University of Alberta Exp Medical Science	Canada
	Ana Sofia	Correia	Neuronal Survival Group, Lund University	Sweden
	Peter	Ebbesen	Laboratory for Stem Cell Research	
	Eskil	Elmér	Experimental Brain Research	
	Katarina	Emanuelsson	Cellartis AB	Sweden
	Jantine	Freeman		Canada
Dr	Peter	Freeman	EuroStemCell Project Manager, University of Edinburgh	UK
Dr	Christof	Friedrich	European Patent Office	Germany
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	Vanessa	Hall	Dept of Experimental Medical Science, Lund University	Sweden
	Lars	Hareng	ECVAM (JRC)	Italy
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Dr	Peter	Höglund	Department of Rheumatology, Lund University Hospital	Sweden
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	Lena	Jonsson	Ministry of Health and Social Affairs, Stockholm	Sweden
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	Tomas	Leanderson	Immunology Group, Lund University	Sweden

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	Rui Lui G	Reis	Group of Policy Advisors, European Commission	Belgium
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Prof	Elisabeth	Rynning	Department of Law, Uppsala University	Sweden
Prof	Nils-Eric	Sahlin		
	Magnhild	Sandberg-Wollheim	Lund University	Sweden
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