Biobanking Pluripotent Stem Cell Lines: UK and EU regulations
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April 1st 2013 – NIBSC will become part of the Medicines and Heal-care products Regulatory Agency

National Institute for Biological Standards and Control
Assuring the quality of biological medicines
Aspects of “Regulation”

- Statutory regulatory framework for human embryos and other human tissues and derived cell lines
- Non Statutory regulation for stem cell lines
- Role of UKSCB in delivering stem cell lines for clinical applications
- Research using stem cell lines
Tissue & Cell Products: Transplantation vs Cell Culture

- Minimal Processing (e.g. bone marrow, cord blood)
- Human Tissues/stem cells

\[ \text{in vitro} \text{ cell culture} \]
Regulatory and Guidance Documents

Statutory legislation:

• The Human Fertilisation and Embryology Research Purposes Regulations (2001)
• The Human Tissues Act (2004 & 2008)
• The Human Fertilisation and Embryology Act (1990 & 2008)
• The Human Tissues (Quality & Safety for Human Applications) Regulations (2007)
• Clinical Trials Regulations EC (2004)
• Advanced Therapy Medicinal Products Regulations (1394/2007/EC)

Codes of practice and guidance:

• HTA Codes of Practice e.g. Imports/export of human tissues,
• JACIE (HSC, FAHCT)
• The Code of Practice for the Use of Human Stem Cell Lines (2004 & 2010) (non-statutory)
• International Stem Cell Banking Initiative – Principles of best practice for banking testing and distribution of hESCs for research – Andrews et al., SCRR 2009
UK Regulatory Framework

Governance for embryonic stem cells in the UK is:

• Both statutory and non-statutory
• Dependent on use (i.e. solely for laboratory research or clinical therapy)
• Dependent on intent (i.e. the future use of the cells)

Statutory control for all cell types is vested in three Regulatory Agencies:

• Human Fertilisation and Embryology Authority (HFEA)
• Human Tissue Authority (HTA)
• Medicines and Health-care products Regulatory Agency (MHRA)

Non-statutory control is vested in the UK Steering Committee for the UK Stem Cell Bank and the Use of Stem Cell Lines
‘The UK Steering Committee for the UKSCB and for the Use of Stem Cell Lines’

- Examine and approve all research utilising human embryonic stem cell lines (Ethics)
- Approve all applications to deposit or access stem cell lines from the UKSCB
- Promote voluntary Code of Practice for the ethical use of human stem cell lines in research and clinical practice
- Oversee:
  - import and export of hESC lines
  - activities of the UK Stem Cell Bank

- Intended to promote public confidence in hESC research
- hiPSC excluded (UKSCB manages hiPSC banking)
UK Regulatory Map for Stem Cell Research and Therapy

1. IVF or CNR
2. Stem Cell line
3. In vitro Stem cell research
4. Animal Research (Chimeras)
5. Clinical Trials
6. Product license

Pre-Clinical

Clinical

Regulators

HFEA
REC
HTA
UK Stem Cell Bank Steering Committee
Home Office

R&D Activity

GTAC
MHRA
EMA

Statutory oversight
Voluntary oversight
Mechanisms for Delivery of ATMPs

- Clinical Trials – under MHRA in UK
- Market Authorisation of new products - EMA issues product licenses
- Cell therapies based on individual patient needs:
  - Hospital exemptions
  - ‘Specials’ arrangements
Role of UKSCB under Code of Practice

• To bank or curate all human embryonic stem cell lines generated in the UK (HFEA license condition)
• To bank, test and release well-characterised and ethically-sourced adult, foetal and embryonic stem cell lines
• International supply of cell lines at “Laboratory Grade” and “EUTCD Grade” as starting material for human application
• To work with the academic, clinical, commercial, regulatory and policy-setting organisations to support translational research in regenerative medicine
• To develop and disseminate best practice in the culture, testing, characterisation and preservation of stem cell lines
“Clinical Grade” Cell Banks?

Seed stock of “undifferentiated” cells

UKSCB: Suitable evidence to take forward for development for clinical application: traceability/documentation

GMP Master/Working Cell Bank of “undifferentiated” cells

GMP Partially differentiated/progenitor cells (banked or part of manufacturing process)

GMP differentiated cell product
UKSCB EUTCD Grade

• ‘EUTCD Grade’:
  – Meet requirements of UKSCB ‘due diligence’ evaluation process: as appropriate compliance to progress for development of clinical applications
  – Not qualified for use in any specific clinical application and not for direct use in patients

• Human application of ‘EUTCD Grade’ cells:
  – Requires careful review and development by user:-
    • Product specific risk assessment
    • Cell line and process development
    • GMP master and working cell banks
  – Requirements will vary depending on: patient cohort, production process, therapeutic protocol, biological characteristics etc.
hESCreg Database for Europe (NB now hPSCreg)

- Provide scientific and ethics data on cell lines
- EC Tool: hESCs approved for use in EC research (scientific, regulatory and ethical review)
- c700 lines currently including hiPSCs
- Now a ‘proving house’ for hiPSCs

http://www.hescreg.eu/
Conclusions

• Use of *in vitro* culture brings new challenges (e.g. contamination, stability)
• Research developments very close to clinical application = Risk for the whole field!
• But need to make progress (not everything is manufactured under “GMP”)  
• Careful *science-based evaluation of risk* is vital 
• Key issues in standardisation for ATMP product specification: *purity, identity, potency*?