Registries and Biobanks for Human Stem Cell Lines

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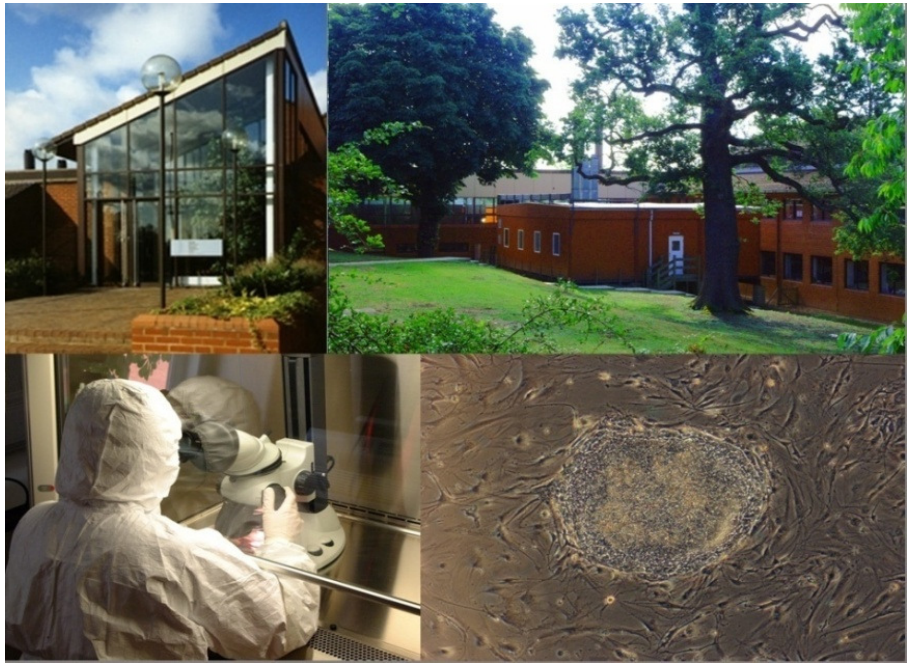
ESHRE Course, Valencia, 8th November 2010



National Institute for Biological Standards and Control
Assuring the quality of biological medicines

Overview

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- Registries and ‘Biobanks’
- Case study - the hESCreg registry
- Biobanks and their operation
- Case study – UKSCB
- iPSC banking

Registry vs ‘Biobank’

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Registry: data source

- Lists of nationally approved embryonic stem cell lines to address public concerns (NIH, MRC, RKI, ISCIII....)
- Sources of information on each cell line (hESCreg, ISCI, UMass. etc.)

Biobank: cell source (physical store of cell lines)

- Various levels of operation
- NB care with link between published data, registry data and the actual cells

Coordination of Cells and Data?

LINK?

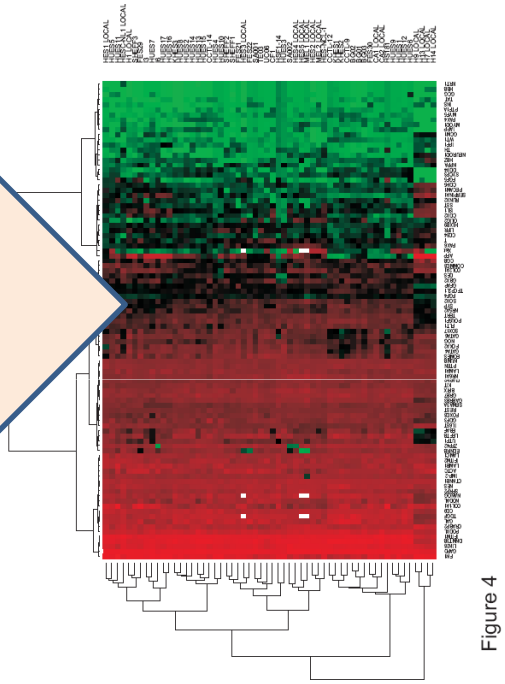

Figure 4

- Crosscontamination/switching
- Biological variability - differentiation, passage level, culture system/media
- Microbiological contamination

NB Documented traceability between cells and data

Registry Quality

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- Large number of cell line entries - not necessarily a mark of value – scientific and ethical scrutiny are vital (quality of science and public acceptability)
- Hazards – wrong data provided, data entry errors, ageing data sets, stability of electronic data files, unauthorised interference/'hacking'
- How does the registry manage these?
- Are there formal documented management processes?

hESCreg database www.hescreg.eu

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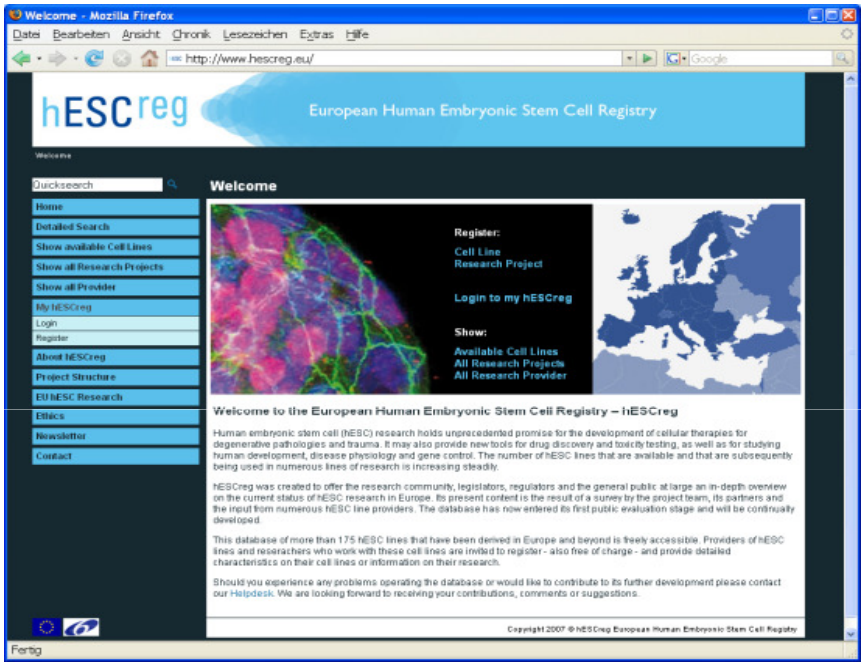

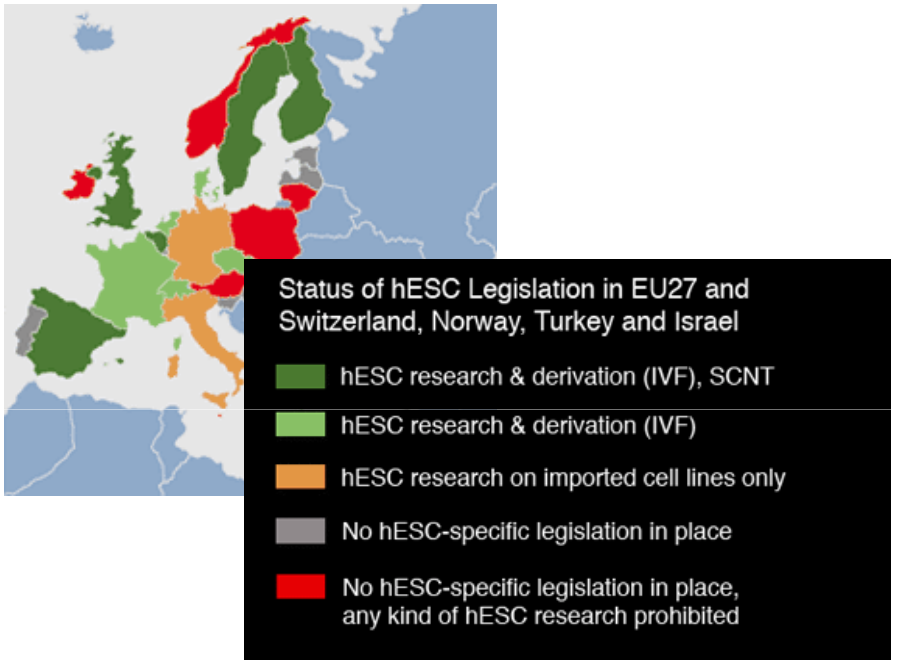

hESCreg: >600 lines registered from around world (iPSC)

EC reference point: acceptability for use in EC research

Others: WiCell, UKSCB, ICSCN, ISSCR, UMass

hESCreg: Key Features

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- Code of Practice: aims and operational principles, structure, function, obligations and dealing with risk
- Protocols: SOPs for data acquisition, data entry, authorisation and review
- CoP and SOPs published on website www.hescreg.eu
- Review by originator, country reps (StC) and SAB
- Independent biobank data (WiCell, UKSCB ....)
- However, not practical to validate information – ultimately reliant on provider accuracy and honesty

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Biobanks: Part of the Stem Cell Community

Biobanks: Role in Stem Cell Research

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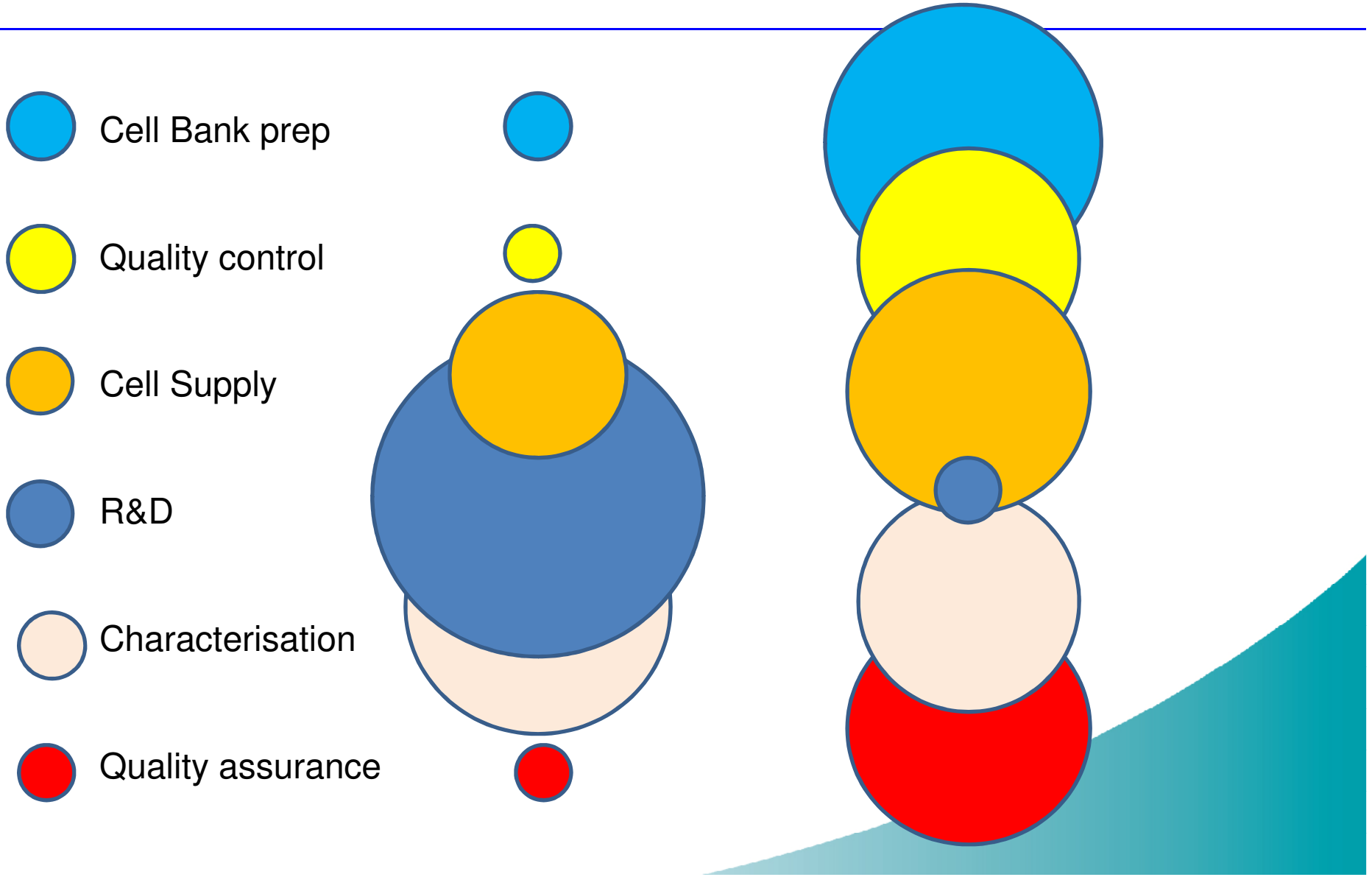
- Scientific standardisation:
  - Focussed on core QC (contamination, identity)
  - Same stocks distributed to many labs and over time
  - Pristine and traceable early passage material retained for future
- Safety:
  - Centralised testing not always possible in individual laboratories
- Ethical issues:
  - Centralised processes in biobanks can assure ethical issues addressed
- International coordination:
  - Common standards to promote quality of science and support for research and clinical application

“BioBanks?”

Local/collaborator supply	National/international distributor



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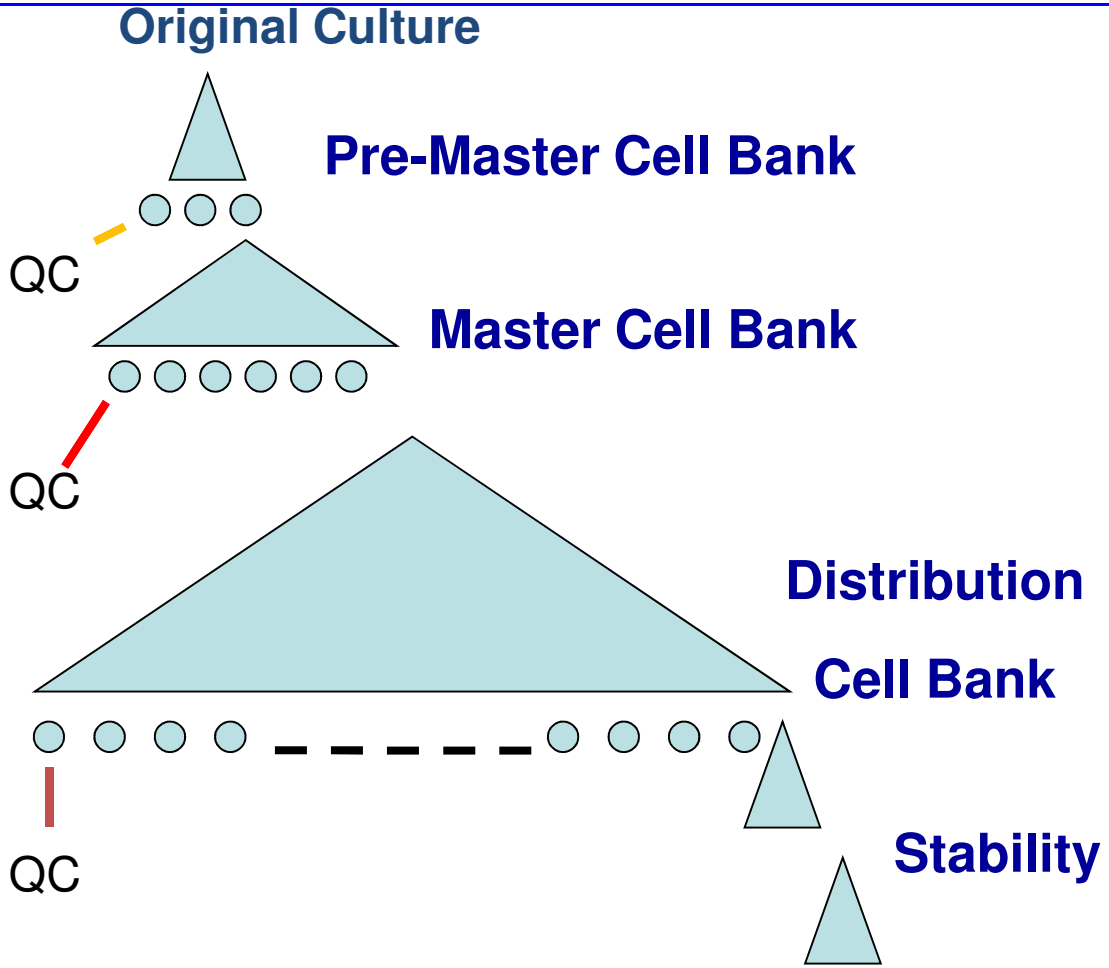
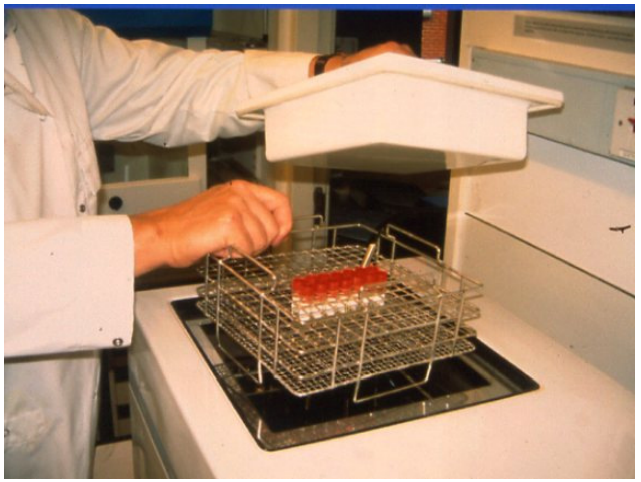
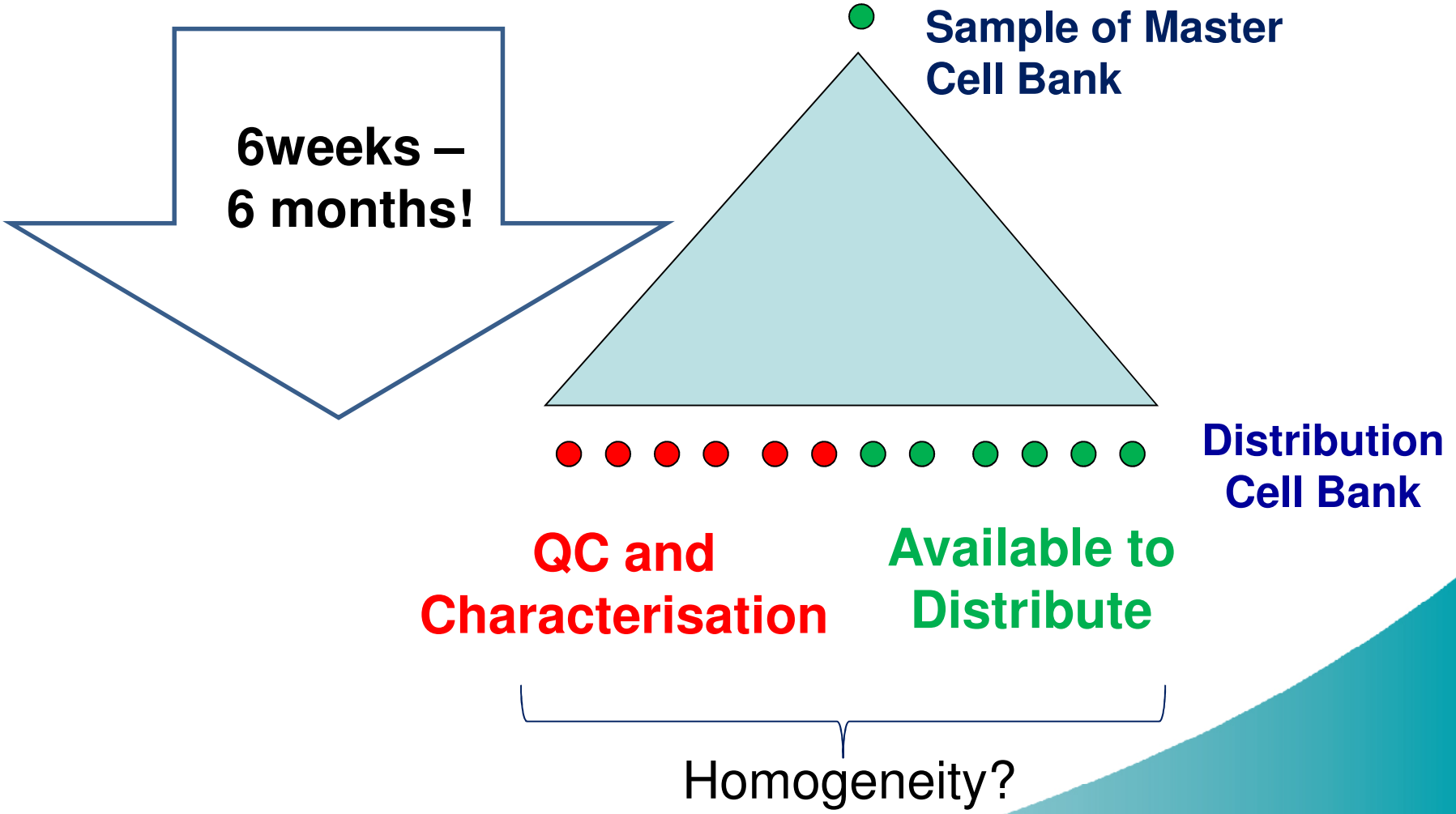
The Banking Process: Technical Issues

The Banking Process





The Banking Process:
- Variable Cell Growth
- Need for Robust Quality Control/Characterisation



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BioBank Case Study – UK Stem Cell Bank:

- Accession of cell line

- Banking/QC/Release Process

- Storage and Distribution

UKSCB: How it Works

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Operational principles:

- Provision of ethically sourced stem cell lines for ethically approved research and clinical trials
- High degree of transparency (CoP)
- Prohibited from discovery research and product development IP

Immediate benefits:

- Cells are banked, tested and distributed at no charge with depositor IP protected
- A neutral partner in the stem cell field coordinated with regulators (e.g. WHO, EMA) and long experience in standardisation of biological medicines .

Accession of Stem Cell Lines: Getting the cells and the right information

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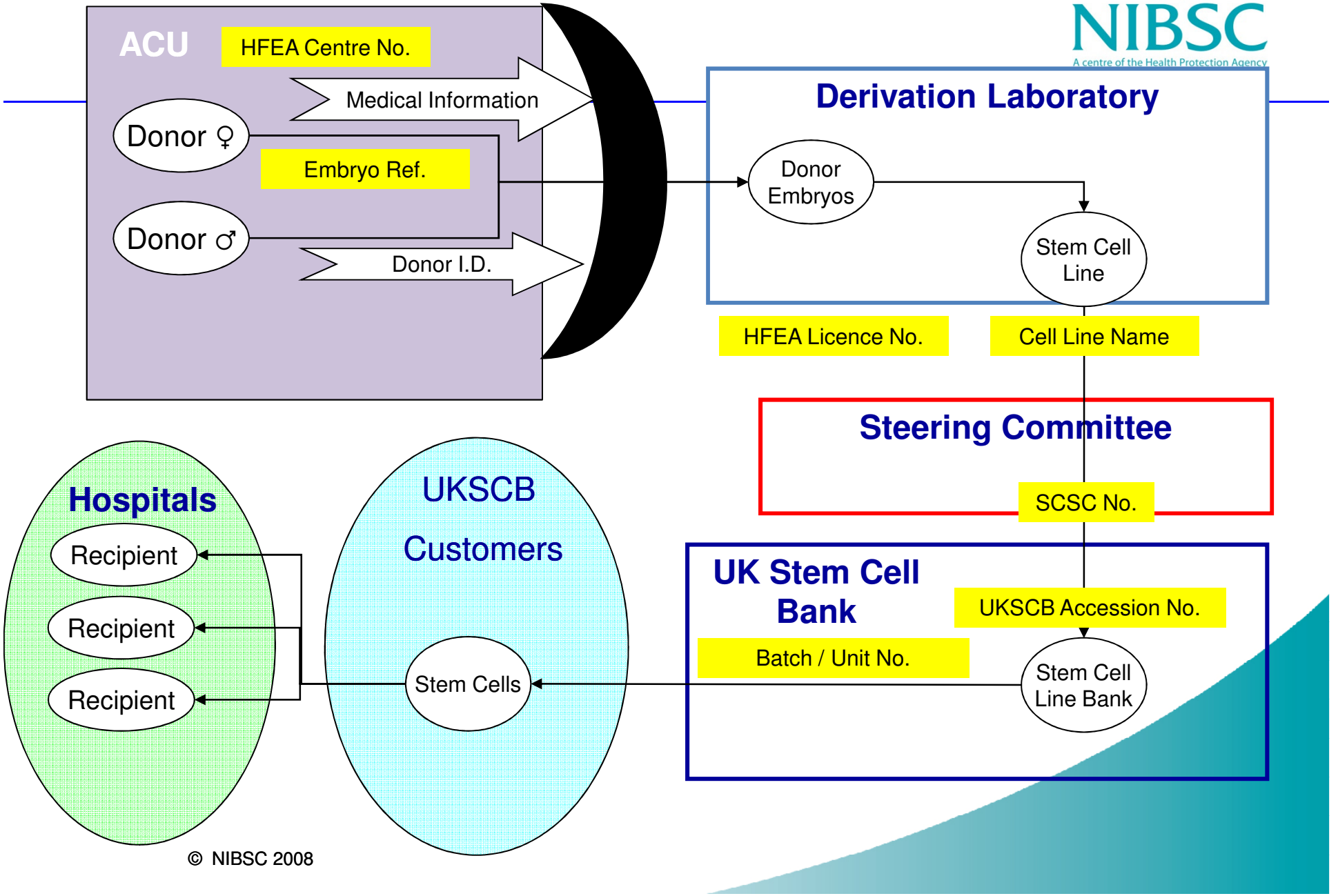
- Obtain intra-lab consensus: culture, preservation characterisation (may be challenging!)
- Evidence for consent and ethical approval for derivation (HFEA and Steering Committee)
- Additional requirements for clinical grade cells:
  - HTA (EUTCD) - provision of starting cells,
  - MHRA/EMA - clinical trials and product
  - Key elements :
    - Traceability (SOPs, reagents, environment, staff)
    - Donor selection and anonymised link to donor
    - Risk assessment

Traceability for hESC Lines



Banking and Shipment Processes

- Traceability is critical
- On- and off-site GMP storage
- Document procedures, environment/staff, testing to enable demonstrate of what the Bank did:
  - Research lines - dealing with complaints and trouble shooting
  - Clinical trials – Serious Adverse Reactions & SAEs
- Ensure recipient use is appropriate: UKSCB SC ethical review of use of hESCs – challenge for international supply
- Qualified shipment equipment and carriers

Quality Control and Characterisation: Are the Cells What They Should Be ?

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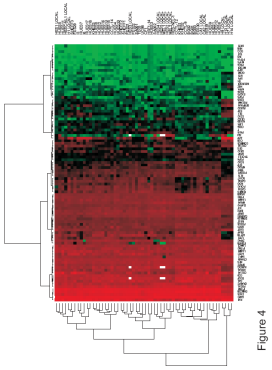
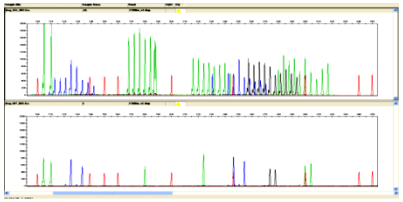
- Correct phenotypic and function
  - Surface markers,RNA, differentiation/pluripotency?

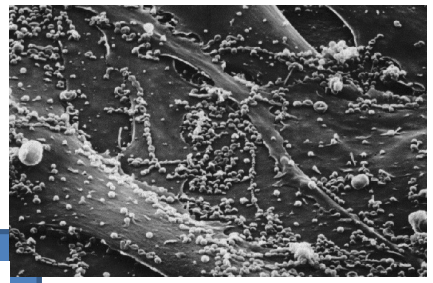


ISCI

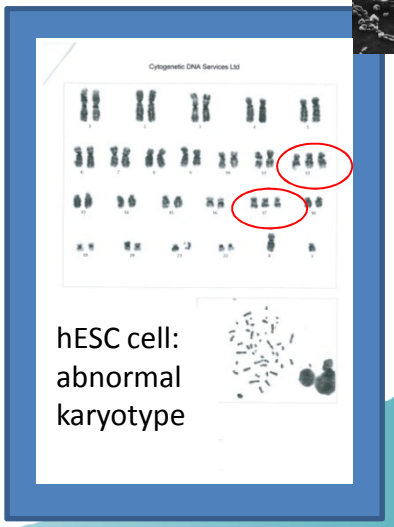
- Correct identity
  - DNA profile



- Absence of microbial contamination
  - Original tissue, cell culture contaminants



- Stability of *in vitro* cultures:
  - Passage
  - Culture conditions



New UKSCB Laboratories

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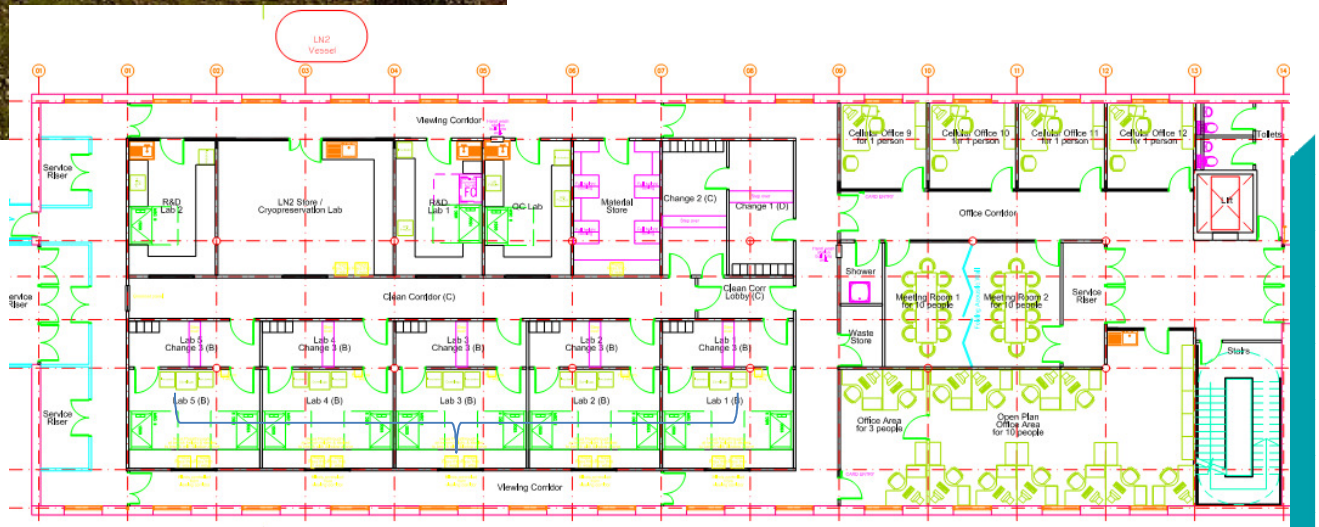
UK StemCellBank



Clinical grade (EUGMP)
Analytical labs
Safe depositary
Hotel laboratory

Induced Pluripotency Stem Cell Lines

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- Exciting opportunities with large banking initiatives being launched
- Scientific challenges:
  - Same technical difficulty as hESCs
  - Reprogramming may variable – need lab assay to screen “iPSC” lines for complete reprogramming and pluripotency
  - Safety issues for clinical application
- Ethical challenges:
  - Use of foetal tissue
  - Publication of genetic data: donor privacy and medical/social implications for donors
- Need to establish technical and ethical standards: good efficient science and public acceptability NB UK experience with unconsented use of tissues

Added Value from Stem Cell Banks

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- Improve access to qualified lines (reduce need to derive new hESCs, qualification of iPSC lines)
- International coordination (ISCBI, ISSCR, EWP etc.) e,g. ISCBI Guidelines for hESC procurement, banking, testing and distribution (Stem Cell Reviews and Reports, Dec. 2009)
- Supporting depositors: resolve contamination, cell identity, altered characteristics, lost cells!
- Research not the priority: Focus on the technical improvement and validation of methods
- Technical back-up and training

Conclusions: Current Challenges

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- Changing science, ethics, regulation
- Commercial issues:
  - Rapid turnover of ownership,
  - MTAs under old legislation/regulation,
  - Demands for exclusive ownership of lines versus altruistic donation of embryos for broad research?
- Maintaining relevance of cells: new growth conditions and characterisation methods – rebanking!
- Clinical grade cells? (ISCBI/EWP)
- iPSC: important but care: "frying pan to fire"?