ToxBank


Deliverable D4.6

# Points to consider in gaining access to human tissue and cell lines.


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## Contents

## 1. Executive Summary

The ToxBank data warehouse provides a web accessible shared repository of know-how and experimental results to support the SEURAT-1 cluster in developing a replacement for *in vivo* repeated dose toxicity testing. The information within the ToxBank data warehouse is uploaded from the research activities of the cluster partners as well as relevant data and protocols from other sources, such as public databases. The data is collected to enable a cross-cluster integrated data analysis eventually leading to the prediction of repeated dose toxicity. The warehouse should continue to provide access to this knowledge after SEURAT-1 for academic and industrial uses, as a potentially self-sustainable operation.

ToxBank is being developed to manage and provide access to all protocols and experimental data across SEURAT-1 to support an integrated data analysis. In addition to this it promotes standardisation across SEURAT-1 and in particular a number of deliverables relating to best practice are being established including a summary of considerations in gaining access to human tissues and cell lines which is presented in this Deliverable report which is made available through the ToxBank Wiki (www.toxbank.net).

## 2. Introduction

The following report outlines the points to consider when accessing human tissues and cells for use in SEURAT-1 projects. It encompasses and expands on a number of ToxBank deliverables that promote the dissemination of best practice in the areas of quality and regulatory standards and draws on principles established to underpin the delivery of robust, reproducible and reliable biological assays which are enshrined in established published best practice documents for the use of tissues and cell cultures (e.g. UKCCCR (2000); Coecke, et al., (2005); ISCBI (2009). Special considerations may also be required for acquisition of cells of reproductive origin and the reader is referred to guidance such as that published by Franklin et al. (2008).

This document assumes that the laboratories involved in the SEURAT-1 cluster work to endorse these concepts and practices through fit-for-purpose facilities, with trained staff and suitable documentation.

This document addresses key areas of consideration common to all partners in the SEURAT-1 cluster when sourcing tissues and cells and should provide a template against which an assessment can be made of the suitability of the biological material for partner projects. We note that legislation and guidance may be provided on a national basis, and local rules applied in the researcher's organization. These should be considered dominant over any specific indications in this document.

# 3. Issues for accessing human tissues and cells

## 3.1 Infectious hazards

Biosafety is a primary consideration when sourcing human tissues, primary cells and cells. The handling of these tissues and cells is governed by local and national legislation and guidelines. In general there is no requirement to test for the presence of adventitious agents in human cells or tissues used for research. However there are a number of suppliers of tissues that test donors for a range of blood-borne viruses prior to the harvesting of tissues and cells and these tests are specified on cell and tissue information sheets (Appendix 1).

Prior to starting work with biological material a risk assessment should be made to identify and evaluate the risks and put in place a framework to ameliorate or reduce these risks. The evaluation should consider risks of all procedures from receipt to disposal of cell and tissues and include potential risks during the processing of the tissue which in addition to the biological hazards might also include and chemical or physical risks.

Staff should be appropriately trained with training and competency documented in formal training records. Staff should be provided with suitable facilities and equipment to contain potential microbial contamination and prevent cross-contamination of other tissues and cells being processed.

## 3.2 Consent

It is pivotal that partners using cells and tissues in the SEURAT-1 cluster ensure that the consent for the use of this biological material is fit for the purpose. This issue has been addressed in ToxBank deliverable D4.4 under the 'Ethical Issues' section of the 'Evaluation form for suppliers of Cell Lines'.

In addition, a 'Risk Evaluation Form' (Appendix 2) was produced for the SEURAT-1 project, SCR&Tox in the form of the Operational Sub-Deliverable 1.1.1 'Banking and Release of Caucasian hESC Lines' which addressed a number of issues to be considered during the evaluation of the consenting process for cell lines for use in SEURAT-1. These considerations form the basis of the questions below and can be modified to apply to tissues, primary cells and cell lines and to meet additional local requirements.

### Consenting process

The following are a series of questions that can be addressed by those responsible for obtaining consent that will help give some assurance that the requirements of ethical review boards have been addressed. These questions have been set up with special reference to isolation of stem cell lines from the donated tissue.

i. To your knowledge was fully informed consent obtained and recorded for the donor tissue or donor tissue used to generate the cell line? **Yes/No**

ii. Has the donor been anonymised? **Yes/No**

iii. Have you attached:
   - **a.** a copy of the original consent form with donor identity blanked out? **Yes/No**
   - **b.** a blank copy of the consent form? **Yes/No**
   - **c.** an English translation of the consent form? **Yes/No**
   - **d.** a copy of information provided to the donor? **Yes/No**
   - **e.** a statement from a person authorised by the owner or centre where the tissue was procured or the cell line was derived indicating a contact and reference for the cell line that would facilitate confirmation of the origin and nature of the original consent**. Yes/No**

iv. As part of obtaining consent was the donor notified of the following:
   - **a.** That the tissue or derived cell lines may be exploited commercially and that they would not receive any personal financial benefit in relation to the use of the cells **Yes/No**
   - **b.** That donation and information derived from their tissue or cell line would not directly influence their personal future treatment? **Yes/No**
   - **c.** That there would be no feedback to them on donor? **Yes/No**
   - **d.** That the tissue/cells and/or derived cell lines could be used for a wide range of purposes in many labs? **Yes/No**
   - **e.** That derived cell lines may be tested for genetic characteristics and microbiological agents? **Yes/No**

v. Constraints on use of tissue or cell lines:
   Did the donor request any constraints on the use of the donated tissue or derived cell lines? **Yes/No**

If any of the responses to sections i–iv are no, then these items should be discussed with the local ethics committee. If the answer to section v is yes, the details of any constraints should be investigated so that the impact on the use of any derived cells or cell lines is understood and that third parties who may receive the materials are also aware of these constraints and comply with the donor requirements.

It is important to note that if appropriate informed consent is not obtained then this can adversely affect the use of the biological material. Indeed, in the case of a pluripotent cell line this could prevent an assay/test developed in the Seurat-1 cluster from being suitable for adoption by other partners including commercial application. Anyone seeking to establish consent or reviewing consent for tissue or derivation of cell lines should also check their own local and national rules and regulation to ensure that the informed consent and proposed use of cells and tissues is compliant.

### 3.3 Traceability and documentation:

Traceability is key to assuring the appropriate provenance of cells and tissues used for biological assays. This is achieved by the implementation of a documentation system to track the cells and tissues from procurement to use in an assay. Accurate records for all stages of this process will often be documented in forms, standard operating procedures etc., and these can also be used to facilitate the analysis and replication of laboratory work. Templates for documenting the tissues used in experimental work can be found in Coecke et al. (2005). The stages of the process should be mapped out to include procurement, receipt of biological material, processing the material, performing assays using the material and finally, disposal of the materials. Documentation should be put in place to cover the complete process.

### 3.4 Tissue sampling and delivery process

The process of sampling of tissue and its transport to the laboratory is vital to the success of any subsequent laboratory use. It is helpful to establish a formal protocol for tissue supply that is agreed with the medical and/or nursing staff involved and local safety advisors (Stacey et al., 1998). This should include:

- The selection of donors to ensure the tissue is suitable and does not carry exceptional microbiological risks.
- Description of tissue required, means of sampling, container type, storage medium and labeling (to assure patient names are not used).
- Arrangements for storage, collection and shipment.

The protocol should also state who has responsibility for each of these stages and it may be helpful if the receiving laboratory arranges for supply of distinctively labeled containers to avoid use of inappropriate transport media.

The manner in which the tissue is handled, stored and transported must ensure:

a) sustained viability and functionality of the cells,
b) prevention of environmental microbial contamination and

c) avoid conditions that would promote growth of potential endogenous microbial contaminants.

Other guidance on the general principles and practice of this aspect of tissue procurement and safe handling of cells and cell line is given in Stacey et al., (1998).

### 3.5 Obtaining cells and tissues from Biobanks

Professional bodies such as the American Association for Tissue Banks and European Association for Tissue Banks support development of best practice for clinical tissue banks, and cells and tissues supplied for clinical use are regulated in Europe under the European Union Tissues and Cells Directive (EUTCD) (COMMISSION DIRECTIVE 2004/23/EC; 2006/17/EC and 2006/86/EC,) . A number of international documents on 'best practice' in biobanking have been published on fundamental aspects of tissue and cell banking by the Organisation for Economic Co-operation and Development, (OECD) (2007 and 2009, http://www.oecd.org/,); and by the International Society for Biological and Environmental Repositories, (ISBER, http://www.isber.org/ ) (2012).

Numerous organisations supply tissue for clinical and or research use. The European project Biobanking and Biomolecular Resources Research Infrastructure, (BBMRI) (**www.bbmri.eu**/), has established a network of tissue and biomaterial storage centers, supplying materials for research use. A number of commercial companies also supply donated human cells and tissue for research (see Appendix 2) and these companies often supply internationally.

It is important that suppliers of tissue meet the key aspects of best practice as outlined in this section and procure according to local and national requirements. In ToxBank, a supplier's register and supplier selection process have been developed (see Appendix 1& D1.4.5) to assist in this process.

### 3.6 Acceptance of tissue

Cells could be received into the laboratory in many forms such as whole tissue, growing cultures and cryopreserved cells. As part of the quality control for cells and tissues to be deemed 'fit for purpose' for use in assay systems, a set of acceptance criteria should be established for each type of biological material. Such criteria will include:

- Confirmation that material has traceability to consent
- Condition of the material. Since viable material forms the basis of most biological assays the viability of the cells needs to be established and the cells accepted as 'fit for purpose' or rejected on the basis of their viability
- Transportation, time in transit and storage conditions .

- A number of parameters need to be examined to authenticate the cells. These include, identity, characterisation

This selection process will facilitate the standardisation and reproducibility of the cells and acceptance criteria will vary depending on the critical parameters for their analysis and use.

### 3.7 European laws and regulations

The procurement and use of tissues, primary cells and cell lines are subject to a number of laws and regulations. When intended for use in humans the required standard is the European Union Tissue and Cells Directive (EUTCD), (COMMISSION DIRECTIVE 2004/23/EC; 2006/17/EC and 2006/86/EC), which regulates the appropriate procurement processing, testing, storage and supply. For non-clinical purposes, permission to obtain and supply will reside with the local research ethics committee (LREC) who will typically issue approval based on the justification for the work and employment of suitable ethics procedures. In some countries such as the UK, when the LREC approval expires any retained tissue will need to be stored in a licensed tissue establishment. In the UK this license is issued by the Human Tissue Authority (HTA) and details of the UK licensing and exemptions can be found on the HTA website (http://www.hta.gov.uk/).

Requirements for import and export of human tissues for clinical use are also addressed under the EUTCD and in addition, national laws may apply on import and export of human cells and tissues for research and other uses e.g. UK regulations implemented by the HTA (see above), French human tissues regulations implemented by The French Biomedicines Agency (Agence de la Biomedicine). An extensive document, the International Compilation of Human Research Standards (2013 Edition) produced by the Office for Human Research Protections, U.S. Department of Health and Human Services, has been 'developed for use by researchers, IRBs/Research Ethics Committees, sponsors, and others who are involved in human subjects research around the world', and provides a comprehensive source for the laws, regulations, and guidelines that governs this type of research in 104 countries. It also provides information on accepted national and international standards.

# 4. Special issues for human and animal cell lines

### Human cell lines

Points to consider in procuring and banking human embryonic stem cell lines have been published in ISCBI (2009) and a European/US consensus on more general issues for best practice in their use were published by Coecke et al., (2005). ToxBank has produced a registry of suppliers of human cell lines and human pluripotent stem cell (hPSC) lines (Appendix 1) and an evaluation form to apply to any cell lines intended for use in Seurat-1 (Appendix 2). In addition the ToxBank deliverable D4.2 'General Quality and Regulatory Criteria for establishment and Dissemination of hPSCs' describes such criteria applied more broadly to human pluripotent stem cells (for copies of this document see ToxBank data warehouse or contact Dr B Hardy (b.hardy@douglas-connect.com) and Dr G Stacey (glyn.stacey@nibsc.hpa.org.uk). Specific points to consider for the quality control and use of hPSC lines in toxicology have also been described by Pistollato, F. et al (2012).

### 4.2 Non-human cells and tissues

Traceability to an ethically sound source of animal tissues is also an important element in all toxicology work to ensure tissues and cells have come from animal colonies with appropriate husbandry practices which should include the adherence to best practice for management of animal colonies including highly trained staff, suitable ethically approved procedures and appropriate facilities providing for :

1) control of live animals entering and leaving the colony,
2) environmental control and cleaning regime,
3) prevention of infection ingress and spread,
4) maintaining animal mental health
5) procedures for ethically acceptable sacrificing and disposal of animals

For further guidance on this aspect of tissue supply the reader is directed to the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) (http://www.nc3rs.org.uk/category.asp?fid=1&catID=42) for requirements in the UK, under European law (2010/63/EU)., which include advice for husbandry of a variety of laboratory animals and codes of practice for management of animal colonies. The Federation of Laboratory Animal Science Associations FELASA (http://www.felasa.eu/) also provides information and 'represents common interests in the furtherance of all aspects of laboratory animal science (LAS) in Europe and beyond'.

Certain species will be registered as "endangered" under the international CITES agreement and in addition to live animals both tissues and cells from such species will

also be subject to these controls. CITES is the Convention on International Trade in Endangered Species of Wild Fauna and Flora. Its aim is to ensure that international trade in specimens of wild animals and plants does not threaten their survival. Whilst this is unlikely to apply to animal colonies used in toxicology work it may apply to certain cell lines from more unusual species (e.g. the primate cell line B95-8). Details of the CITES agreement and the list of registered species can be obtained at http://www.cites.org/eng/disc/what.php.

### 4.3 Recombinant cell lines

Recombinant organisms may present certain safety hazards for humans or the environment. Accordingly, in Europe there are laws governing the use of recombinant organisms in the laboratory which mean that their creation, use, storage and disposal must be authorised, performed and documented under the applicable regulation. For more information the reader is directed to Coecke et al., 2005; and more recent EU legislation such as European Directive 2009/41/EC.

It is important to check whether a cell line intended for research carries recombinant DNA introduced by non-natural mechanisms and if so to ensure compliance with the national regulation which may include application to the national health and safety regulatory body to obtain permission for the work. Certain genetic modifications which have occurred without use of recombinant DNA technology, such as EBV transformation and creation of cell hybrids including hybridomas, are excluded from such regulation.

## 5. Conclusion

In conclusion this report has set out the points to consider when gaining access to human tissues and cells for use in the SEURAT-1 cluster projects. These objectives will facilitate best practice in the area of assay development promoting the establishment of robust, reproducible and reliable biological assays.

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Pistollato, F., Bremer-Hoffmann, S., Healy, L., Young, L. and Stacey, G., 2012. Standardisation of pluripotent stem cell cultures for toxicity testing, *Expert Opinion On Drug Metabolism and Toxicology*, Feb, 8(2):239–57.

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The French Biomedicines Agency (Agence de la Biomedicine) http://www.agence-biomedecine.fr/About-us?lang=fr

OECD (2007) Best Practice Guidelines for Biological Resource Centres
http://www.oecd.org/sti/biotech/oecdbestpracticeguidelinesforbiologicalresourcecentres.htm
http://www.oecd.org/sti/biotech/38777417.pdf

OECD (2009) Guidelines on Human Biobanks and Genetic Research Databases
http://www.oecd.org/sti/biotech/guidelinesforhumanbiobanksandgeneticresearchdatabaseshbgrds.htm
http://www.oecd.org/science/biotech/44054609.pdf

ISBER, 2012. Best Practices for Repositories: Collection, Storage, Retrieval, and Distribution of Biological Materials for Research. *Biopreservation and Biobanking* 10, pp. 81-161 http://www.isber.org/bp/documents/ISBERBestPractices3rdedition.pdf

Directives

DIRECTIVE 2004/23/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2004:102:0048:0058:en:PDF

COMMISSION DIRECTIVE 2006/17/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 8 February 2006 implementing Directive 2004/23/EC of the European Parliament and of the Council as regards certain technical requirements for the donation, procurement and testing of human tissues and cells http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2006:038:0040:0052:EN:PDF

COMMISSION DIRECTIVE 2006/86/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 24 October 2006 implementing Directive 2004/23/EC of the European Parliament and of the Council as regards traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cell

http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2006:294:0032:0050:EN:PDF

DIRECTIVE 2009/41/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 6 May 2009 on the contained use of genetically modified micro-organisms http://www.biosafety.be/PDF/2009_41_EN.pdf?REQUEST=Seek-Deliver&COLLECTION=oj&SERVICE=eurlex&LANGUAGE=en&DOCID=2001l073p0032

DIRECTIVE 2010/63/EU OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 22 September 2010 on the protection of animals used for scientific purposes http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2010:276:0033:0079:en:PDF

# 7.Appendices

## Appendix 1 – Registry of suppliers

Tissues, primary cells and cell lines should be identified and judged as fit for purpose according to a set of pre-determined criteria. The biomaterial may be supplied via a hospital , by a commercial tissue and/or cell supplier or via a biobank. The following tale gives a list of suppliers of cell lines and tissues.

| C ollection Name | Website | Location, Host Organization | Date Opened |
|---|---|---|---|
| **DSMZ**<br>(Bacterial and fungal strains. Human, animal and plant cell lines. Plant viruses and antisera. Bacterial genomic DNA ) | http://www.dsmz.de/ | Inhoffenstraße 7B<br>38124 Braunschweig<br>GERMANY<br>**Phone**: +49 (0) 531 26160<br>**Fax**: +49 (0) 5312616-418<br>**E-mail:**<br>contact @ dsmz.de<br>Member of the Leibniz Association | 1969<br>(http://www.dsmz.de/about-us/portrait-of-the-dsmz/history.html) |
| **Culture Collections Public Health England**<br>(Cell lines & Hybridomas, DNA & RNA products, Bacteria, Plasmids & Mycoplasmas, Fungi, Viruses) | http://www.culturecollections@phe.gov.uk | **Culture Collections**<br>Public Health England<br>Microbiology Services<br>Porton Down<br>Salisbury<br>SP4 0JG<br>UK<br><br>**Sales & General Enquiries**<br>**Tel:** +44 (0)1980 612512<br>+44 (0)1980 612512<br>**Fax:**<br>+44 (0)1980 611315<br>**Email:**<br>culturecollections@phe.gov.uk<br><br>**Technical Support**<br>**Tel:** +44 (0)1980 612684<br>+44 (0)1980 612684 | 1984<br><br>Public Health England is the custodian of four unique collections that consist of expertly preserved, authenticated cell lines and microbial strains of known provenance for use in medical science and laboratory healthcare. |

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| | | **Fax**: +44 (0)1980 611315<br>**Email:** culturecollections.technical@phe.gov.uk<br>A business unit of the Health Protection Agency, UK | |
| **ICLC**<br>(Animal cell lines, including cells of human origin and hybridomas, are accepted for patent deposit.) | http://www.iclc.it/ | ICLC Interlab Cell Line Collection<br>Istituto Nazionale per la Ricerca sul Cancro c/o CBA<br>Largo Rosanna Benzi, 10<br>Genova (GE)<br>16132 Italy<br>**Tel**: +39-0105737 474<br>**Fax:** +39-0105737 295<br>**E-mail**: iclc@ist.unige.it<br>The National Institute for cancer Research of Genoa | 1994 |
| **UK Biobank**<br>(A major national health resource, and a registered charity in its own right, with the aim of improving the prevention, diagnosis and treatment of a wide range of serious and life-threatening illnesses – including cancer, heart diseases, stroke, diabetes, arthritis, osteoporosis, eye disorders, depression and forms of dementia.) | http://www.ukbiobank.ac.uk/ | UK Biobank<br>1-2 Spectrum Way<br>Adswood<br>Stockport<br>SK3 0SA<br>**Tel**: 0800 0 276 276 (free from most UK land lines) or +44 (0) 2920 765597,<br>UK Biobank is hosted by the University of Manchester and supported by the National Health Service (NHS). | 2006 |
| **ALSPAC**<br>(The Avon Longitudinal Study of | http://www.bristol.ac.uk/alspac/ | Children of the 90s<br>Oakfield House<br>Oakfield Grove<br>Bristol | 1991 |

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| Parents and Children (ALSPAC) provide a vast amount of genetic and environmental information which is assisting scientists all over the world with research into a wide range of health problems.) | | BS8 2BN<br>**Tel:** +44 (0) 117 33 10010<br>Hosted by University of Bristol | |
| **UK Human Tissue Bank**<br>(UKHTB offers a range of fresh and frozen human tissues, cells and sub cellular fractions for research.) | http://www.ukhtb.org/ | The UK Human Tissue Bank Innovation Centre,<br>De Montfort University,<br>Oxford Street,<br>Leicester LE1 5XY<br>**Tel:** + 44 (0) 116 250 6014<br>**Fax:** + 44 (0) 116 250 6015<br>Based at De Montfort University in Leicester | 1999 |
| **Cellartis**<br>(Biotechnology company focused on pluripotent stem cells and technology for drug discovery research, toxicity testing and regenerative medicine) | http://www.cellartis.com/ | Cellartis AB<br>Arvid Wallgrens Backe 20<br>SE-413 46 Göteborg<br>SWEDEN<br>**Tel:** +46 31 758 09 00<br>**Fax:** +46 31 758 09 10<br>**E-mail:** info@cellectis.com<br>Part of the Cellectis stem cells Business Unit | 2001 |
| **UKSCB**<br>(A repository of human embryonic, foetal and adult stem cell lines, including iPSC lines) | http://www.ukstemcellbank.org.uk/ | UK Stem Cell Bank<br>National Institute for Biological Standards and Control<br>Blanche Lane<br>South Mimms<br>Potters Bar<br>Hertfordshire<br>EN6 3QG<br><br>**Tel:** +44(0) 1707 641000<br>**Fax:** +44 (0) 1707 641050<br>**E-mail:** enquiries@ukstemcellbank. | 2002 |

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| | | org.uk<br><br>Hosted by NIBSC, funded by the Medical Research Council (MRC) and the Biotechnology and Biological Sciences Research Council (BBSRC). | |
| **Lonza BioResearch**<br>(Primary & Adult stem cells, Pluripotent Stem cells, Cell culture products, Assay solutions, Nucleic Acid & Protein Electrophoresis, qPCR) | http://www.lonza.com/Home.aspx | Europe Middle East Africa<br>United Kingdom<br><br>Customer Service<br>**Tel:** 0808 2349 788<br>**Fax**: 0808 2349 778<br>**E-mail:** order.uk@lonza.com | |
| **Asterand**<br>(Global provider of high quality well characterized human tissue and human tissue-based research solutions to drug discovery scientists. | http://www.asterand.com/Asterand/ | Asterand USA<br>TechOne Suite 501<br>440 Burroughs<br>Detroit, MI 48202-3420<br>United States<br>**Tel**: + 1 (313) 263-0960<br>(US Toll Free) 1.866.3TISSUE<br>**Fax:** +1 (313) 263.0961<br>Asterand Europe<br>2 Orchard Road<br>Royston, Herts<br>SG8 5HD<br>United Kingdom<br>**Tel:** +44 (0) 1763 211600<br>**Fax:**+44 (0) 1763 211555 | 2006 (as a merger between Asterand & Pharamagene. More recently, July 2012, Asterand has merged with Stemgent) |
| **Biopredic**<br>(Providing Human & animal primary cells, cell lines, tissues for Research, drug discovery, drug development, Pharmacology and toxicology) | http://www.biopredic.com/ | Biopredic International<br>8-18 rue Jean Pecker<br>35000 RENNES - FRANCE<br>**Tel:**+ 33 (0) 2 99 14 36 14<br>**Fax** + 33 (0) 2 99 54 44 72 | 2006 |
| **Cellular Dynamics**<br>(Develop and deploy a | http://www.cellulardynamics.com/products/i | Cellular Dynamics International | |

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| number of cell types derived from iPS cells to aid drug discovery and toxicity testing, including iCell Cardiomyocytes, human heart cells, iCell Endothelial Cells, human blood vessel cells, and iCell Neurons, human brain cells) | ndex.html | 525 Science Drive<br>Madison, WI 53711<br>**Tel:** +1 (608) 310-5100<br>US Toll-free: (877) 310-6688<br>Japan: +81 75 256-8582 | |
| **Riken Bioresource centre**<br>(Global center for collecting, preserving and providing bioresources) | http://www.brc.riken.jp/lab/cell/english/ | Cell Bank, RIKEN BioResource Center<br>3-1-1 Koyadai, Tsukuba, Ibaraki, 305-0074, Japan<br>**Fax :** +81-29-836-9130<br>**E-mail**: cellbank@brc.riken.jp | 2001 (http://rtcweb.rtc.riken.jp/English/out/out.html) |
| **WiCell**<br>(Banking,cytogenetic testing and distribution of stem cell lines.<br>Providing clinical grade pluripotent stem cell lines, quality control testing and cell banking services) | http://www.wicell.org/ | WiCell Research Institute<br>U.S. Mail P.O. Box 7365<br>Madison, WI 53707-7365<br><br>COURIER DELIVERY:<br>614 Walnut Street, 13th Floor<br>Madison, WI 53726<br>General Information<br>Tel: (888) 204-1782<br>E-mail: info@wicell.org | 1999 |

All released materials are subject to completion of a Material Transfer Agreement (MTA) or Terms & Conditions. One supplier of human embryonic stem cell lines, UKSCB, also applies an ethics review process of the intended research overseen by a National ethics review body.

## Appendix 2- Evaluation of sources of cell lines

The ToxBank deliverable D4.4 'Establishment of an Evaluation Process for Supplies of hPSCs' comprises an evaluation form for human cells and cell lines being selected for use in Seurat-1. This form covers ethical issues, commercial issues, banking, testing and characterization. These broad headings could be applied, in principle, to any tissue or cell type and the form could be adapted accordingly.

# Evaluation Form for Suppliers of Cell Lines

**Supplying laboratory should be asked to complete the following sections to show how the supplier meets the criteria for supply of human cells and cell lines**

**Ethical Issues**

**How does the supplier address the requirement that:**

1) for each cell line there is traceability to fully informed consent on the original tissue without exposing the identity of the donor.

| |
|---|
| *Evidence of an appropriate ethics review can be given such as a reference number or code on the US NIH, UK Steering Committee or hPSCreg registries* |

2) any constraints implemented on the use of the cells are documented and made available to recipients of lines?

| |
|---|
| *Describe how donor constraints would be recorded in information on the cell lines you supply and how recipients are notified so that inappropriate use of cell lines can be avoided* |

**During the consenting process was the donor aware that:**

1) derived lines may be exploited commercially but that donors would not receive personal financial benefit.

| |
|---|
| *Answer Yes or No and then give wording used in consent or provide a blank copy of the consent form used* |

2) derived hPSCs could be used for a wide range of purposes in different laboratories and may be tested for genetic characteristics, microbiological contamination and other features of the cells.

| |
|---|
| *Answer Yes or No and then give wording used in consent or provide a blank copy of the consent form used* |

## Commercial Issues

How does the supplier identify the owner/s of the cell line and whether permission has been granted by the owner/s or their agents for the intended use or is the line released for general research without constraint (see also ethics criteria re: donor constraints).

How does the supplier assure that the intellectual property rights relating to each cell line or any components used to derive the cell line (e.g. DNA constructs) are clear and would not influence their use for commercial application?

*The supplier is not expected to be aware of all IP that applies to a cell line or its use, such as patents. However, the supplier should explain how ownership of the cell line and any technology used to generate it (such as reprogramming method and/or vectors) are communicated to the recipient and how such ownership issues are managed, attaching a copy of any relevant transfer agreements.*

**What constraints does the supplier place on commercialisation of the cell line?**

*Provide a copy of the Materials Transfer Agreement that will be in place between supplier and recipient and/or describe nature of uses to which cell lines can be put*

**How does the supplier record and/or publish information on the derivation procedure for each cell line?**

*Provide a copy of the Materials Transfer Agreement that will be in place between supplier and recipient and/or describe nature of uses to which cell lines can be put*

## Banking (culture, preservation and storage)

Does the supplier operate a tiered banking system for supplied cells and how does this meet the recommendations in ISCBI (2009) for

1) Procurement of Cell Lines

*Write and outline description of the process used for procurement of lines and their banking*

2) Cell Banking Procedures and Documentation

*Write and outline description of the process used for procurement of lines and their banking*

3) Cell Bank Quality Control

*Give a list of QC and characterisation tests performed routinely on released cells and complete the table (below) indicating in each case the specific method used (include any SOP reference), the release criteria (e.g. "no visible bacterial or fungal growth" for a sterility test) and whether each one is performed under a quality system and accreditation scheme. Add extra sections to the table if required. An example of information for the table is as follows.*
*Identity of cell line*
*Method and controls: STR profiling of cell line DNA isolated from a bank cryovial in parallel with a HeLa cell control. Test performed by an external contractor wit GLP accreditation for the test.*

*Release criteria . Profile distinct from any other cells supplied*

4) The Process of Releasing Cell Banks

*Answer yes or no to indicate whether there is a process which releases each cell bank produced for distribution and if answering yes give details of the formal release process and how it is documented including an explanation to show that cells with failed QC could not be released*

**Testing and Characterization**

Please complete the following table to explain how the supplier completes quality control and characterisation:

| Test | Specific Methods and controls used | Release criteria |
|---|---|---|
| **Identity of cell line** | | |
| **Karyotype** | | |
| **Sterility (bacteria/fungi)** | | |
| **Mycoplasma** | | |

| | | |
|---|---|---|
| **Viral contamination** | | |
| **Post-thaw recovery** | | |
| **Pluripotency** | | |
| **Growth characteristics** | | |
| **Antigen expression** | | |
| **Gene expression** | | |
| **Genetic stability** | | |

END of document