# POLICIES AND PROCEDURES

## 1. MISSION

The mission of Massachusetts Human Stem Cell Bank (MHSCB) is to serve as a source of high quality, well characterized human pluripotent stem cells, including human ES and reprogrammed (iPS) cell lines, for the biomedical research community. This resource is intended to facilitate research that will advance our understanding of human development and disease pathogenesis as well as explore potential therapeutic applications of pluripotent stem cells in the treatment of diseases.

## 2. DEVELOPMENT AND FUNDING

The MHSCB, a component of the UMass Human Stem Cell Bank and Registry (UHSCBR), was established in November, 2008 and is operated by the Office of the Vice Provost for Research of the University of Massachusetts Medical School on its Shrewsbury, Massachusetts campus.

The UMass Human Stem Cell Bank and Registry was developed and is currently operated through funding from the Massachusetts Life Sciences Center (MLSC), a quasi-public agency created by the legislature of the Commonwealth of Massachusetts to support life sciences in the Commonwealth. It receives no NIH funding currently.

## 3. OPERATIONAL GUIDANCE

Banking operations of the MHSCB conform to the banking guidelines established by the U.S. National Academies' (NAS) *Guidelines for Human Embryonic Stem Cell Research*, including 2007 amendments, and the International Society for Stem Cell Research (ISSCR) *Guidelines for the Conduct of Human Em**b**ryonic Stem Cell Research*, 2006. Specifically, the MHSCB intends to conform with these guidelines with respect to both hESC and iPSC lines, as recommended in the NAS 2008 amendments. Operations will also abide by the laws of the Commonwealth of Massachusetts and all applicable Federal laws, including all NIH regulations and guidelines that may apply. In addition, the MHSCB will comply with the terms of the Depository Agreement entered into with each depositor and the terms of the Materials Transfer Agreement with each recipient institution.

Laboratory procedures of the MHSCB adhere to the International Stem Cell Banking Initiative's Guidance, 2008 and comply with Good Laboratory Practices and all applicable laws.

## 4. GOVERNANCE

In accordance with NAS and ISSCR guidelines, banking operations are governed with input from the following committees:

**UHSCBR Scientific Advisory Board (SAB)** – The SAB is comprised of 30 members, both within and external to UMass, with expertise in stem cell biology, medicine, ethics and law. The SAB provides advice on the strategic direction of the UHSCBR as well as providing input on laboratory protocols and procedures for the receipt, banking and distribution of stem cell lines. The SAB receives periodic reports and requests for input on the activities of the Bank and convenes at least once per year to evaluate the overall progress and direction of the UHSCBR.

**MHSCB Oversight Committee (OC)** – The OC is an internal UMass committee that is responsible for providing oversight of activities and advice to the MHSCB staff on an ongoing basis.

**Massachusetts Life Sciences Center (MLSC)** – As the funding agency for the UHSCBR, the MLSC and its Scientific Advisory Board receive quarterly reports of UHSCBR activities. The MLSC provides input on the

overall mission and direction of the UHSCBR and periodically reviews banking operations and progress.

**UMass Embryonic Stem Cell Oversight (ESCRO) Committee** – Although not involved in the day-to-day activities of the MHSCB, the UMass ESCRO Committee serves as an important resource to offer guidance to the MHSCB. The ESCRO Committee has reviewed and approved the MHSCB operations that involve teaching and training activities involving use of hESCs.

## 5. BANKING PROCEDURES

The MHSCB banks and distributes ethically sourced pluripotent stem cell lines that are of value to the biomedical research community. The Bank is currently not accepting adult stem cells or materials such as bone marrow or cord blood for banking. The MHSCB is currently not equipped to bank or distribute clinical grade cell lines for use in clinical research or therapeutic applications.

Pluripotent cell lines currently accepted for banking in the MHSCB:

- Human Embryonic Stem Cells (hESCs)
- Reprogrammed Stem Cells – such as Induced Pluripotent Stem Cells (iPSC), especially unique lines such as those derived from individuals with specific genetic diseases.

Appropriate safeguards will be used to protect the privacy of donors. A secure system for protecting the privacy of donors when materials retain codes or identifiable information will be developed. Therefore, at this time, UHSCBR will only accept stem cell lines of donors having no such codes or individually identifiable private information.

The MHSCB will not conduct any derivation of new lines, although investigators in the University may do so in University laboratories, which activities are separate and independent from the MHSCB operations. These University investigators are subject to the same MHSCB procedures and requirements as investigators from outside of the University.

### 5.1 Cell Line Quality Control and Characterization of Banked Cell Lines:

The MHSCB has a well-trained and experienced technical staff responsible for expansion, cryopreservation, quality control and characterization of banked cell lines. All standard operating procedures are available at the MHSCB website (www.umassmed.edu/MHSCB).

Quality control and characterization assays performed on banked lines include, but may not be limited to:

- Mycoplasma testing
- Karyotyping
- Genotyping
- Immunocytochemical analysis of stem cell markers
- qRT-PCR analysis of gene expression
- Flow cytometry analysis of cell surface markers
- Embryoid body formation and analysis for pluripotency

### Certificate of Analysis

Once newly deposited cell lines have been characterized and the MHSCB review is complete, the MHSCB Laboratory Director issues a Certificate of Analysis summarizing the characteristics of the cell line as observed by the MHSCB at that time. The MHSCB Laboratory Director posts this Certificate on the MHSCB website and provides a copy of the issued Certificate to the Cell Line Originator. A blank certificate is available on the MHSCB website.

As the MHSCB develops its standards for examining the characteristics of the deposited cell lines (pluripotency, purity, etc.), these will be published and/or made available on the MHSCB website.

### 5.2 Depositing Cell Lines in the MHSCB

Expansion and creation of distribution lots of cell lines deposited at the MHSCB is based on anticipated need in the research community. Acceptance of a cell line for banking does not constitute an agreement to expand the cells. The MHSCB retains the authority and judgment as to whether a deposited cell line will be banked by the MHSCB. For example, a cell line may be rejected for banking if prior culture conditions or other attributes do not meet the MHSCB's standards.

The MHSCB's priority is to make NIH approved cell lines available to the research community. At the current time, the MHSCB intends to receive only frozen vials of cells that do not include individually identifiable donor information and which are research-grade and not clinical-grade cells..

For each depositor submission, all forms, agreements and documentation are assigned a unique submission code which tracks the forms in the MHSCB records system using bar codes and other technology. If the cell line is accepted for distribution, the submission code is then associated with the vials received and the MHSCB bank code number assigned to the cell line. The information includes the documentation of the provenance of the cell lines, including form of donor informed consent and confirmation that the consent applies to that cell line, documentation of IRB and ESCRO Committee approval, and Simple Letter of Agreement that records any donor restrictions and whether any reimbursements or payments were made to donor.

**Assessment of Restrictions on Use**

One key aspect of the submission process is the identification by the depositing institution of what are the restrictions on use that apply to the cell line proposed to be deposited with the MHSCB for banking. This information is essential for ensuring that the cells are used in accordance with the wishes of the original donor. Also, it is needed to allow requesting institutions to determine whether the cell lines can be properly used in accordance with applicable laws that may apply to their jurisdiction (such as laws that prohibit or limit payments to donors). The MHSCB uses this information to determine whether to accept the cell line for banking. For example, the MHSCB will not accept cell lines which can be linked to a donor. The MHSCB will not accept cell lines for which the donor has forbidden redistribution by the depositor. Further, at this time, the MHSCB will not accept cell lines for which the donors have retained the right to withdraw the cell lines or cell lines or for which the donor has required that the cells be destroyed after a specified period of time.

**Required Forms and Documentation:**

**Bank forms:**

- Depositor guidance document - explains the deposit process.
- Cell line submission form – communicates developer and cell line information to the bank.
- Simple Letter of Agreement (SLA) – To ensure adherence to applicable guidelines, laws and regulations by institutions and researchers requesting stem cell lines. The SLA describes the restrictions on use required by the donor.
- Depository Agreement (DA) – Legal agreement of conditions for transfer of cells for banking.

**Required Depositor Documents** (described in greater detail on submission forms)**:**

- Blank informed consent form for the submitted cell line.
- Proof of IRB or equivalent approval of procurement process.
- Statement of approval or non-applicability from ESCRO Committee or equivalent.

**Cell Line Deposit Procedure**

1. Cell line depositor obtains forms for cell line deposit from the MHSCB website.
2. Depositor completes forms and other required documents and submits to Bank (as specified on

Required Information Checklist).

3. The Bank Administrator reviews forms to ensure completion and contacts depositor for missing information if needed.
4. Application is sent to the Compliance Officer (CO). CO performs initial review of submission documents to ensure all required documents and information have been submitted correctly and that proper authorizations are in place. CO will review documentation to ensure that restrictions noted on the deposit form, consent form and ethical review form/letter are included in Simple Letter Agreement.
5. CO confers with the Lab Director to ensure that there is sufficient information for culturing and banking of cells. Clarification and concerns about application are communicated to Administrator, who would contact depositor for additional information.
6. Signed DA is reviewed, approved and signed by University Technology Transfer Office (Office of Technology Management or OTM) if no action is required. Clarification and concerns about the DA are communicated to the depositor's Technology Transfer Officer or other authorized representative of depositor.
7. OTM sends copy of signed DA to CO.
8. CO certifies that application is complete and notifies Lab Director of the final approval and cell line is given a MHSCB bank code.
9. Lab Director sends shipping label and instructions to depositor.
10. Lab Director documents receipt of cells for banking.

### 5.3 Requesting Cell Lines from the MHSCB

Cell lines banked at the MHSCB will be provided to researchers at academic and non-profit institutions solely for teaching, academic, non-profit, or other non-commercial internal research purposes. No cell lines will be distributed to for-profit companies.

The cell lines that are available for distribution are described in detail on the MHSCB website. Each has a MHSCB code assigned to it.

The cell line recipient is solely responsible for securing all reviews and approvals required by applicable treaties, laws, regulations, guidelines and institutional policies. However, a request for cell lines must be accompanied by a copy of these approvals.

The stem cell line may be the subject of a patent application or covered by patent rights in one or more countries. No express or implied licenses or other rights are provided to the recipient under any patents, patent applications, trade secrets or other proprietary rights of the cell line developer, depositor or any third party. The cell line recipient is solely responsible for all legal compliance and for obtaining any necessary licenses to third-party rights, such as any patent or proprietary rights of third parties relating to use of the cell line.

Each cell line banked at the MHSCB and available for distribution shall have a Certificate of Analysis (CoA) associated with it (see 5.1 above for more detail). The CoA summarizes the characteristics of a specific distribution lot of that cell line, as determined by the MHSCB staff. However, the CoA is not a guarantee or warranty of any kind. The cell lines are frozen by the MHSCB for distribution and must be managed with a great degree of skill to be properly thawed and useful. The thawed cell lines may or may not exhibit the characteristics described in the CoA. At time of distribution, the passage number of a cell line at time of shipment is recorded in the MHSCB records.

**Fee Schedule:**

The current fees associated with the delivery of cell lines are listed below. These fees cover only a portion of the MHSCB's actual banking and characterization costs for each cell line. Payment is due once all the required documentation is complete and received by the MHSCB, including complete and proper execution of all documents. All prices listed are US dollars.

| | hESC | iPSC |
|---|---|---|
| **Academic Internal** | $400 | $600 |
| **Academic External** | $600 | $1000 |
| **Commercial Research** | $1000 | $1500 |

Please note that the recipient is also responsible for all shipping charges for the requested cells. Shipping costs may be billed through the MHSCB or charged directly to recipient accounts.

**Required Forms and Documentation:**

**Bank Forms** (available on website)**:**

- Requestor guidance document - explains the request process.
- Cell line request form
- Simple Letter of Agreement (SLA) – To ensure adherence to applicable guidelines, laws and regulations by institutions and researchers requesting stem cell lines. The SLA documents restrictions on use required by the donor.
- Materials Transfer Agreement (MTA) – Legal agreement of conditions for transfer of cells from the bank to the requestor.
- Payment of transmittal fee for each vial.

**Required Investigator Documents:**

- Principal Investigator Curriculum Vitae (CV)

**Cell Line Request Procedure**

1. Investigator obtains cell line Request Form from Bank website.
2. Investigator completes Request Form and all other required documents (as specified on the Request Documentation Checklist) and submits these to the Bank.
3. MHSCB Administrator reviews forms and attached documents to ensure completion. Administrator contacts requestor for missing information if needed.
4. Application is reviewed by Compliance Officer. CO will ensure that all required documents and information have been submitted correctly and that proper authorizations are in place. CO will review the PI CV and project description to ensure that the proposed research use is non-trivial. CO will approve and sign if additional information is not required. Clarification and concerns about application are communicated to MHSCB Administrator. Administrator will obtain additional information from requestor before CO signs Request Form.
5. Signed MTA is reviewed, approved and signed by OTM if no additional information is required. Clarifications and concerns about the application are communicated to requestor's Technology Transfer Office or other authorized representative of the requestor's institution.
6. OTM forwards MTA approval to CO.

7. Compliance Officer certifies that application is complete and notifies Laboratory Director /shipping personnel of the final approval.
8. Shipping personnel contacts requestor with shipping details and ships requested cell line and documents that shipment was sent.

## 6. Requestor Obligations

By accepting and receiving stem cell lines from the MHSCB, the requesting investigator and the requestor institution commit to comply with the terms of the Materials Transfer Agreement and the Simple Letter of Agreement that cover the cell line. These terms provide that the original material received by the requesting investigator remains the property of the depositor institution of the cell line originator. The requesting investigator can only re-distribute the cell line in the manner provided for in the MTA and SLA. The requesting investigator must secure all necessary approvals that apply and otherwise abide by the terms of the MTA and SLA before undertaking new research projects.

## 7. Annual Surveys

The requesting investigator commits to complete an annual survey to report whether or not the investigator's research project is continuing, whether the cell line has been cultured and used successfully, whether there are any publications associated with the use of this line, and to confirm that he/she continues to abide by the terms of the MTA and SLA. The annual survey form is available on the MHSCB website.

## 8. Patent Rights

Each stem cell line available for distribution from the MHSCB may be the subject of a patent application or covered by patent rights in one or more countries. No express or implied licenses or other rights are provided to the recipient under any patents, patent applications, trade secrets or other proprietary rights of the cell line originator, depositor or any third party. The cell line recipient is solely responsible for all legal compliance and for obtaining any necessary licenses to third-party rights, such as any patent or proprietary rights of third parties relating to use of the cell line. The MHSCB does not participate or become involved in the negotiations regarding intellectual property rights among cell line originators, depositor institutions or requestors.

The MHSCB fully intends to comply in every respect with the patent laws and all other applicable laws that apply to its operations. The MHSCB is also subject to and shall comply with the terms of any Depository Agreement entered into by the MHSCB with any depositor. Its operations include performing validation and characterization of the MHSCB banked lines. However, the MHSCB laboratory staff do not conduct discovery research on MHSCB banked lines.

## 9. Liability Statement

The MHSCB is responsible for the proper conduct of its operations and carries sufficient insurance or self-insurance as appropriate to cover its operations. The MHSCB is also subject to and shall comply with the terms of any Depository Agreement entered into by the MHSCB with any depositor.

Stem cell lines distributed by the MHSCB are experimental in nature and may have hazardous properties. The cell lines will be supplied to requesting institutions without warranty of merchantability or fitness for a particular purpose or any other warranty, express or implied, and without any representation or warranty that the use of the cell lines will not infringe any patent, copyright, trademark or other proprietary rights.

## REFERENCES AND RESOURCES:

Massachusetts Human Stem Cell Bank: www.umassmed.edu\mhscb

NAS Guidelines for Human Embryonic Stem Cell Research:
http://books.nap.edu/catalog.php?record_id=11278

ISSCR Guidelines for the Conduct of Human Embryonic Stem Cell Research:
http://www.isscr.org/guidelines/index.htm

Massachusetts Life Sciences Center: http://www.masslifesciences.com/

University of Massachusetts Medical School Office of Research:
http://www.umassmed.edu/research/index.aspx