Notes to Researchers

Depositing Stem Cells in the UK Stem Cell Bank

The UK Stem Cell Bank (UKSCB) is part of the Medicines And Healthcare products Regulatory Agency (MHRA) .

The purpose of this information sheet is to provide you with a step-by-step guide to depositing your stem cell line(s) in the UKSCB and the role that you, the Depositor, play in this process.

It is assumed that you will have read the relevant sections of *The Code of Practice for the Use of Stem Cell Lines*. The current version of this document is available on both the UK Stem Cell Bank Steering Committee's website and the UK Stem Cell Bank's websites (NIBSC - UK Stem Cell Bank). It is a requirement that samples of any embryonic stem cell lines derived in the UK under an HFEA licence are deposited with the Bank. Overseas depositors wishing to deposit their lines in the Bank are encouraged to also read the sections of the *Code of Practice* relating to consent and ethical issues.

Step 1 (Embryonic stem cell lines only)

Complete the Application Form. The decision to accept the cell line into the UKSCB is **NOT** made by the Bank but by the *Steering Committee for the UK Stem Cell Bank and the Use of Stem Cell Lines* (the Steering Committee) (UK Stem Cell Bank Steering Committee - GOV.UK (www.gov.uk)) on the basis of the application form you provide, together with any additional information requested by the committee. If you are unsure of anything in the form, you should contact the Secretariat to the Steering Committee at the address given on the form. It is advisable to contact the Secretariat ahead of completing the application form, since they will advise you of any supporting information that may be required by the Steering Committee to assess your application. The same form is used for both Research Grade stem cell lines as well as for those cell lines intended for human application. Such cell lines are termed Clinical Grade by the Bank as they fall under the terms of the EU Tissue and Cells Directives. The Application form to deposit cell lines in the UKSCB can be found on the Bank's website.

The application form should be sent to the Steering Committee Secretariat at the address given and **not** to the UKSCB since this will delay the process of depositing your line.

Step 2 (Embryonic stem cell lines only)

Notification of Acceptance. Once the Steering Committee has approved your application to deposit your cell line(s) in the Bank, both you, as the Depositor, and the Bank will be notified by the Steering Committee Secretariat that approval has been given. At this point the Bank will formally receive your application form and copies of any technical documentation you have provided to the Steering Committee in support of your application.

Though it is likely that the Bank will already have been in contact with you informally prior to formal approval by the Steering Committee, you will also receive a formal notification letter, sent by email from the Bank, informing you that the process of accessioning the stem cell line has begun.

Step 3 (All stem cell lines)

Signing the Legal Agreement. In order for your cell line to be accessioned by the UKSCB, a Materials Deposit and Distribution Agreement (MDDA) must first be signed between the MHRA (the legal entity for the MHRA and the Bank), and the legal representative of the owner of the cell line. The owner of your cell line (and their legal representative) will have been identified in the application form provided to us by the Steering Committee. A standard agreement has been developed and will be shared with you by the Bank. Correspondence either from you or your legal representatives should be addressed to the Bank's whose email address is given in our formal notification letter.

Please note that for cell lines submitted under the HTA Quality and Safety for Human Application Regulations (Clinical Grade cell lines) for human application, the MDDA will contain information about your obligations regarding Serious Adverse Reaction and Serious Adverse Event (SAER) reporting.

Once your legal representative has confirmed acceptance of the agreement and provided information on your legal place of business, we will prepare executable copies of the agreement and send these to you for signature. Three signed copies of this document should then be returned to the Bank. These will be countersigned by us and an executed copy return to the owner of the cell line (or their legal representative).

The legal agreement must be in place before the process of accessioning your cell line can begin. Failure to sign the legal agreement may delay the process of accessioning.

Step 4

Accessioning the cell line(s). The process of accessioning differs depending on whether you are depositing a Research Grade cell line or a cell line intended for human application. However, both require that we gather information from you about your cell line. You will not be asked to supply cells until all the information requested has been provided. The process involves:

- Gathering information on the cell line from you
- Receiving technical training (where required)
- Identifying a stock of cell material for transfer into the Bank
- Undertaking a risk assessment and/or Due Diligence Process

Establishing contact. Members of the UKSCB, together with a member or members of your staff will work together to progress deposition of your cell line(s), ensuring a smooth transfer of the cell line(s) into the Bank and establishing a good working relationship with you. The UKSCB representatives will be drawn from amongst those scientists who will ultimately be responsible for banking your cell line(s). You, as the depositor, should nominate at least one point of contact for the Bank, together with other members of staff who can provide the technical knowledge required for day-to-day culture of the stem cell line(s).

Cell lines intended for human application: In the case of cell lines intended for human application, the Bank must first ensure that, in its opinion, the cell line meets the requirements of the UK Human Tissue Authority (HTA) with respect to the European Tissue and Cells Directives as laid out in HTA guidance documents. This is done by undertaking a process of Due Diligence in which you will be invited to participate.

You will be sent two forms to complete:

- *The Due Diligence Initial Assessment Form*
- *The Cell Line Information Form*

Both forms will be shared with you by the Bank and must be completed before being returned in order for us to begin the review process.

Senior members of the Bank will then review the information you have sent and make a recommendation to the Bank's Designated Individual (DI) who will make the final decision as to whether or not, in the Bank's opinion, the cell line meets HTA requirements. During this review process, the Bank may request additional evidence from you to help clarify the information you have provided. In exceptional circumstances, the Bank may make a request to audit a particular process or processes. However, the Bank will never ask you for confidential patient information that could identify the donors of the original material.

Once a decision has been made, you will be notified by the Bank's DI. In the event that you are unhappy with the decision you may lodge an appeal with the Director of the MHRA for a review of that decision. The Bank will be able to advise you on the mechanism for this.

The HTA require that all cells and tissues for human application are the subject of a Third Party Agreement between the Designated Individual from the depositing centre and the Bank's DI. This Quality Agreement will be sent to your DI once the decision to accession your cell line as Clinical Grade has been reached. This agreement must be signed before we can receive your cell line into the Bank. The Quality Agreement makes reference to the HTA requirements for SAERs reporting within 24 hours. Definitions of SAERs and guidance of how to report an SAER can be found on the HTA website (https://www.hta.gov.uk/guidance-professionals/regulated-sectors/human-application/human-application-serious-adverse-event).

Gathering information. *The Due Diligence Initial Assessment Form* provides information on the cell line's compliance with HTA Directions. The *Cell Line Information Form* provides us with an up-to-date record of how your cells have been derived and cultured and forms the basis of the risk assessment for your cell line(s). These forms will become part of the Cell Line Master File for your cell line: the base document for Quality Assurance and audit of your cell line.

The Bank's representative(s) will work with you to complete these forms, if required. We will also be asking you for copies of any protocols and procedures that you have used in the production of the cell line(s). All protocols and procedures you provide will be treated in confidence, but we would request that you make us aware of any areas that you consider to be commercially sensitive.

Once the forms have been completed, you should check that the details are correct before the relevant personnel sign and return the forms to the Bank.

Additional information related to traceability, materials used in the culture of the cell line and results of QC test undertaken on the cell line will also be requested. A full list of the information required will be provided to you at the time of contact.

Cell lines not intended for human application: Research Grade stem cell lines fall outside the remit of the HTA and are thus not required to undergo the Bank's Due Diligence process nor do they require a third party (Quality) Agreement. However, we will still require information from you in the form of a completed *Cell Line Information Form*

For both Research Grade and Clinical Grade cell lines, the remainder of the process of accessioning is the same.

Identifying a suitable stock of cells for transfer to the UKSCB. The Bank only takes in frozen (or vitrified) material. Ideally, we would like a minimum of six cryovials or straws all frozen from the same passage. Generally, this should be from the earliest passage that you believe best represents the cell line you have derived and which you know is capable of generating a fresh stock of stem cells. There should also be sufficient stock from this passage left over for us to

archive material locally for future reference. The material provided should be from those stocks of cells that were produced and banked under the protocols and procedures that you supplied to the Bank.

We will also discuss with you whether it would be beneficial to bank any feeder cells associated with your stem cell line and, whether it would be beneficial to receive and test (for sterility and mycoplasma) some material in advance of your cell line(s) coming into the Bank.

Undertaking a cell line risk assessment. Once the task of compiling the information on your cell line is completed, the Bank will undertake a risk assessment. This will involve UKSCB staff and advisors and will decide the panel of tests to be carried out on your cell line(s). The UKSCB undertakes a core panel of characterisation and safety tests, but uses the risk assessment to generate its full testing strategy. You, as the depositor, may be asked to provide further information.

Step 5

Receiving cells at the Bank. Prior to taking in the stock of cells, we will discuss with you the best method of shipping the material to the Bank. This may involve us in collecting the frozen cells from you or arranging for collection by a third party. In either case, the cost of transportation will be borne by the Bank.

We may, from time to time during the banking process, contact you with additional technical questions. Also, if you have requested it, we will return a sample from our distribution bank to you for testing. If we find an inconsistency between data you have supplied and data we have generated during quality control testing, we will discuss this with you prior to releasing the cells for use and placing data on the cell line on our website.

Contact Details

For enquires concerning the application process contact:
committeeservicesteam@mhra.gov.uk

For all general enquires regarding the accession process contact:
enquiriesmail@mhra.gov.uk

For specific enquiries regarding your cell line(s) please consult the UKSCB formal notification letter

Check List (Please complete and retain with your records)

Cell Line:_____

Passage # / Lot # / Unit # of cells deposited _____ /_____ / _____ /

UKSCB Accession #. _____

Date Transferred to UKSCB: _____

Step	Completed	Comments
1		
2		
3		
4		
5		