SOP EU-hPSCreg /001
Soliciting Data on Cell Lines

This protocol describes how sources of cell line data are identified for submission to hESCreg in SOP 002.

Protocol

i) New lines for entry are primarily identified by the hESCreg partners including the Committee of National Representatives, but can also be volunteered by researchers.
ii) Approaches are made by the hESCreg coordinator's office to originators of cell lines to invite data entries.
iii) The hESCreg management office determines whether the originator will enter data directly or send raw data or a publication or summary report for the coordinators to use to enter data.

Permitted Sources of Data

a) From originators of cell lines: these are the preferred data providers.
b) From publications: the hESCreg coordinator, or a person authorised by the coordinator, can transfer data from primary publications on cell lines by the originator. These should be seminal publications or other publications from the originating lab and their collaborators. They must be pre-screened on the basis of two criteria 1) confirmation of ethical consent (either from the publication or from directly by the originator) and 2) cell line characterisation reported at a minimum of passage 10.
c) From data sources other than the originators of the line: these are to be approved on a case by case by the HESCreg project management team.

SOP HESCreg /002
Submission of Data Entries

This protocol describes how data entries for each cell line are compiled ready for evaluation in SOP003.

Protocol

i) Each registrant contacts the hESCreg office and supplies their contact detail**s**. When the hESCreg office is satisfied that the applicant is *bone fide* provider (i.e. from a recognised research organisation) the applicant is formally registered by the hESCreg coordinator's office. The registrant chooses a login name and a password to gain access to the data base. This password only enables the originator to create and amend the data entries provided by them. The hESCreg system administration retains complete access to all information entered to safeguard system integrity. Data entries can also be provided on the data template e-file available from hESCreg (data entry form SOP002).

ii) A single data entry is prepared by each provider for each cell line starting with entry of the minimal data set, i.e. the Registration Information. At this stage they must complete the ethics information section in the online entry form on the hESCreg website (NB a cell line cannot be selected for validation without completing the ethical provenance information). Ideally the data is entered by cell line originators but it may also be entered by the hESCreg management team. Registration Information can be modified and updated by the provider only until the point of notification of the coordinator that the data record is ready for submission. At this stage the data entry cannot be considered as validated part of hESCreg data and is marked as 'not validated' by turning 'off' the fifth 'LED' in the Data Indicator Bar.

iii) The person entering data must ensure that the minimal data fields (see definitions) are completed before submission.

iv) Upon completion of the data entry the provider notifies the coordinator who then sends an email to the provider notifying them that their entry will be locked and that the data set will be submitted to the hESCreg review process. The coordinator's office also ensures that there is traceability between the data entry and the data provider.

v) Only lines with complete Registration Information will be submitted for validation. Where Registration Information is incomplete the provider is contacted again by the hESCreg office at each validation round. Data entries that remain uncompleted for a long period of time will be reviewed and resolved by the project management group.

SOP HESCreg /003
Compilation and Quality Control of draft Registration Information data sets

This protocol describes how cell line entries are evaluated with the assistance of the Committee for National Representatives(CNR) and the ethics advisor (EA) and prepared for approval in SOP004.

Protocol 003.1
i) Information entries are categorised according to sources, which may include entries approved by the originator (i.e. standard data entry) or a *bone fide* stem cell bank authorised by HESCreg .

ii) Before entries are approved they are 'locked' (see SOP hESCreg /002) and presented for evaluation by NRC whose feedback is authorised by the project management group. Any subsequent additional data and corrections will be made via the project management group.

iii) Ethical review of data entries.

The specific procedures for these parts of the evaluation and how this is utilised by the project management group is described below.

Committee of National Representatives Evaluation Procedure SOP003.2
The project management office notifies the CNR that cell line entries are ready for evaluation (via a link to a shared are on the hESCreg website) and a deadline is set for completion of the review. Each national contact completes their respective response entries (i.e. cell lines derived in their country) on the shared area documentation and submits their response on a template (Form SOP 3.2 see appendix).

Responses are reviewed at the end of the consultation period. Evaluation is complete when all national contacts have responded.

The project management group coordinator then reviews responses and authorises the evaluation as complete, subject to EA report (SOP003). Where there are issues that require resolution the project management office works with relevant members of the CNR to seek a resolution which is then presented to the project management group.

The project coordinator's office reviews the completed evaluation process and authorise release of the approved data entries onto hESCreg subject to ethical review

Ethics Advisor (EA) Procedure SOP003.3

1. The EA is nominated by the hESCreg management team based on relevant knowledge and experience in ethics and relevant regulatory issues.
2. The EA receives the same notification to carry out a review of the cell line data entries as sent to the CNR but is requested to review specifically only those cell lines where issues regarding ethical provenance have been raised.
3. The EA evaluates relevant data entries regarding ethical provenance. The EA then provides a summary report to the hESCreg management team on the appropriate evaluation template (evaluation form SOP3.2). This report should include a) a statement on acceptability of cell lines based upon hESCreg provenance acceptability criteria (i.e. minimal registration data), b) a commentary on cell lines where information is missing or where there are other notable issues such as patient consent details which restrict certain uses of the cell line.
4. The HESCreg management team annotates data entries accordingly clarifying any issues as necessary with the EA, the NCR and providers of information.

This protocol describes how evaluated cell line data entries are approved and how disputes and appeals following rejection of cell line registration are managed.

1. Incorporation of feedback from committees

i) Lines approved are reviewed by the hESCreg coordinator's office in conjunction with the authorization reports from the CNR and the EA evaluation procedure. Where there are no issues raised by the committees the cell line entries are marked 'validated' by turning 'on' the fourth 'LED' of the DIB in the database by an authorised member of hESCreg staff.

ii) Where lines are approved but, with a qualifying statement this will be established by the Project Management and added to the cell line entry. Any annotation resulting from feedback process is authorized by the project management group

iii) If, in exceptional circumstances, the hESCreg management feel there is need for further clarification, or where the CNR or EA evaluations prove exceptionally problematic, the project management group will seek a resolution in liaison with the National Representatives and the EA or other external experts as necessary.

2. Notification to data providers of approval

i) The hESCreg management team communicate approvals to all lead data authors/data providers by email.

ii) Where data entries are not approved the hESCreg management team may request further information from the provider or advise the provider that their cell line data entry will remain to be marked as 'not meeting Minimum Registration Information" and may be removed from hESCreg ; in the latter case specific reasons for this action will be given. For appeals see 4.2 below. This will be notified to the appropriate EC officer.

3. Final sign off by HESCreg

When step 1 is completed the appropriate electronic Registration Information of the cell line entry is annotated with the date of approval, marked "validated", and 'locked' by an authorised member of the hESCreg staff.

General principles

Any disputes or appeals relating to registration of cell line entries are managed by the project management group. Decisions by the project management group are recorded by majority vote of members. Where there is no majority the project management group chair is invited to give the casting vote regarding cell line data entry to the hESCreg management who will liaise with national representatives, the EA and other experts as they feel necessary, to agree how differing viewpoints should be represented on the cell line data entries or on general areas of the website. In the case of scientific or ethical differences of opinion, then one option would be to present a summary of such discussions on the website with the associated information and committee consensus statement or report. In the case of the National Representatives, for any issues relating to national regulation or law the appropriate formal national authority will be consulted whose position is final.

Rejected or amended data entries

i) Where data entries from protocol 4.1 (part2) cannot be progressed to the validated state, the data project coordinator's office may request further information.
ii) Following consideration the hESCreg management team will make a final ruling on the cell line data entry in question regarding the compliance of the cell line data provided with hESCreg procedures.

SOP hESCreg/005/v4
Implementation of Changes to hESCreg and Periodic Review

Change control procedure for HESCreg

i) Any changes to procedure are evaluated and authorised in project management group and formally documented in the minutes from project management meetings and archived by the hESCreg coordinator's office.
ii) The project management group may seek expert opinions as necessary prior to agreeing any changes to the hESCreg Code of Practice.

Periodic review

The hESCreg management team also coordinates periodic reviews (typically annually) of hESCreg procedures.

Appendix below:

Appendix 1: Template for the Committee of National Representatives and Ethics Advisor Reports (v06.03.14)

Allocated cell line entries allocated for this review
……..

List any data entries that require comment and add comments:

Cell Line ……..

Comments
……
……
……
……
…….

END