EBMT

European Society for Blood and Marrow Transplantation

REGISTRY FUNCTION

Person responsible	Registry Head
Version	8
Last review	06/08/2018
Approved	Registry Committee

All comments regarding this document should be sent to registryhelpdesk@ebmt.org

TABLE OF CONTENTS

The EBMT maintains a Registry which encompasses all haematopoietic stem cell transplant (HSCT) procedures for all indications. It also stores immunosuppressive treatments for bone marrow failure syndromes (ie: aplastic anaemias), cell therapy treatments other than HSCT and donor information pertaining to collection and donor follow up.

1   Registry structure

The EBMT Registry has several components: the content which is made up of all the data that is collected; the hardware and software which make the collection and storing of the data possible; the supporting documentation, and the staff.

1.1   Support structures

The clinical content of the EBMT Registry is decided by EBMT researchers through the Working Parties. The final structure, format and clinical definitions of the data collection forms (DCF) receive additional support from EBMT staff and staff from other organisations that are important stakeholders of the Registry. This is done through recognised structures such as the Registry Committee, the Definitions Group and the Data Registries Group. Final decisions are made by the Scientific Council and the Board of the Association. See our website www.ebmt.org for more details on the organisation structure.

1.1.1   Working Parties (WP)

The EBMT is divided into Working Parties (WP) formed by voluntary representatives of member centres and headed by an investigator elected by the EBMT members. These WPs are proactive in starting studies and assume responsibility for the clinical data that is collected through the design and auditing of the DCF. WPs can request changes to the forms for aspects in their remit. All requests have to be endorsed by the head of the WP and must be accompanied by adequate definitions of the new data items. The WPs have the final decision on clinical content.

1.1.2   Registry Committee (RC)

The function of the RC is to advise on the Registry's functional development within the context of the EBMT Strategy. The Chair of the RC is appointed by the Scientific Council.

1.1.3   Definitions Group (DG)

The DG is made of representatives of the WPs, representatives of national registry data management staff and representatives of EBMT data management staff. The remit of the

DG is to ensure the DCFs are consistent across WP remits, are feasible in terms of work load for centre data managers, are readable and understandable, and are accompanied by appropriate documentation.

1.1.4   Data Registries Group (DRG)

The Data Registries Group is a loose association of those users in the Registry, the WPs, national registries, donor registries, and other collaborators –except the centres- who access the Registry with great frequency. Their main remit is to feedback to the Registry practical issues raised by the use of the Registry tools: internet access, manuals, Data Collection Forms, etc. It is a discussion group with the capacity to raise issues and suggest solutions but has no executive power. It takes a very active role during the Data Management sessions at the EBMT congress and is the main interlocutor when organising data management training.

1.2   Data collection forms (DCF)

The EBMT has four main types of DCF:

- **MED-A for HSCT**, which contains the minimal essential data. All EBMT members that perform transplants need to submit these data to retain full membership.

- **MED-B**, which contains a large amount of disease and HSCT specific data. Although the disease specific Med-B are currently only used for HSCT, they can also be used for the Cell Therapy Registry if applicable.

- **MED-A for Cell Therapy other than HSCT**, which contains the minimal essential data for this type of treatment.

- **Donor Outcome**, which contains minimal essential data to follow stem cell donors.

All forms can be downloaded from:

https://www.ebmt.org/registry/data-collection

1.3   Hardware and software

The data is stored in an SQL Server database, housed in the Leiden University Medical College (LUMC). The internet project management system, ProMISe, is run and maintained by LUMC IT staff in that same location. The EBMT owns the SQL server and database and has a

permanent licence for ProMISe. Ronald Brand, the ProMISe designer, owns the intellectual property of ProMISe.

1.4   Staff

The EBMT Registry Office is located in London and has 6.6 full time equivalent (FTE) staff:

- Registry Head   RH   (1 FTE)
- Data management lead   DML   (0.6 FTE)
- Data quality coordinator   DQC   (2 FTE)
- Business support manager   BSM   (1 FTE)
- Help desk coordinator   HDC   (1 FTE)
- Information analyst   IA   (1 FTE)

In addition to the above, there is a part-time position supporting the AGNIS project

- Information manager   IM   (0.9 FTE)

The following tasks are the remit of the Registry:

1. Designing, creating and maintaining the database infrastructure for the Registry and for the Membership* projects (RH, IA)

2. Designing and formatting the paper DCF for the Registry (IA, DML, RH)

3. Writing, editing and maintaining the Data Management pages of the EBMT website (DML, RH)

4. Editing and maintaining the Clinical manuals and reference documents (DML, RH, DQC, HDC)

5. Writing, editing and maintaining the technical manuals for ProMISe (DML, DQC)

6. Liaise with WPs for the design of the DCF (DML, RH)

7. Coordinate and interpret requests or queries from centres and submit them to the DG (all)

8. Coordinate and participate in the DG meeting (RH, BSM, DML)

9. Coordinate and participate in the DRG meeting (all)

10. Specialised data entry for difficult data items (ie: corrections.). (DQC, DML, HDC)

11. Requesting follow up and missing data (DQC, DML, HDC)

12. Generate, maintain and process general data quality procedures (DQC, DML, HDC, IA, RH)

13. Send regular information to the centres on the extent of their data registration by type, disease and year (Summary report) (RH)

14. Write and distribute the Data Management News (DML)

15. Provide regular information to the EBMT Board on the level of data registration (Registry tracking) (RH)

16. User management (BSM, HDC, DML, DQC)

17. Administration of National Registry and Study Group permissions (BSM, HDC, DML, RH)

18. Helpdesk service for all matters associated to the Registry (HDC, DML, DQC)

19. Organise the Data Management training sessions at the Annual conference (DQC, DML, RH)

20. Coordinate, provide or support training for data managers (all)

21. Support Study coordinators in the use of the Registry for specific studies (all)

22. Support external collaborators with specific projects (IM, DML, RH)

23. Provide amalgamated reports on request for Corporate sponsors (RH)

24. Provide reports on request for centres (DML, HDC, RH)

The Membership database contains details on all members of the EBMT. This project is essential to the whole EBMT, including the Registry, as it is the source of all the necessary contact details. The project is under the remit of the Executive Office, but the technical support is provided by the Registry office.

The Registry office also suggests and implements procedures to improve data flow, data quality and provide data management support to centres.

2 Use of the Registry

The main function of the Registry is to collect pertinent and good quality clinical data. The main use of these data is clinical research, but it will also be used to support the mission of the EBMT in aspects such as the inspection, auditing and accreditation of transplant centres.

2.1 EBMT led studies

This is the single most important use of the Registry data. The EBMT registry can use all the data submitted to them. It is understood that data submitted to the EBMT can be used for research and published by the EBMT WPs as long as the existing **Guidelines for the Conduct of Registry Studies using the EBMT Registry Database** and the **Authorship guidelines for EBMT publications** are followed. Both documents are mandatory reading for any WP investigator wishing to perform a registry study. Although the EBMT Registry Office has the primary responsibility for cleaning, and updating the data, the EBMT study coordinators contribute to this for specific studies.

2.2 Centre

Member centres use the Registry to store their own data while simultaneously making it available to the EBMT. Each EBMT member can be considered as the main owner of their data, although it is understood that the ultimate owner is the patient. Members submitting data can use their own data for their own purposes without having to require permission or notify the EBMT. Members have access to their own data at all times and can actively block access to selected patients by other authorised users.

2.3 Donor registries

Donor Registries can use the Registry to store their own data while simultaneously making it available to the EBMT. Donor Registries submitting donor data can use their own data for their own purposes without having to require permission or notify the EBMT. Donor Registries have access to their own data at all times.

Donor registries may also request access to the Registry in order to follow the donors or the patients that have received donations from them. In the latter case, the centre has to give permission for the donor registry to be able to see selected patient data.

2.4 Study groups

Groups of centres can set up studies and use the EBMT Registry as their database. This is made by a request that the EBMT sets up a study group and its corresponding series of permissions to access the data. Such requests have to be submitted together with explicit permissions from the principal investigators of the involved centres. All centres must be

members of the EBMT. A procedure document with a request form template is available for this purpose.

2.5 National registries

National registries operating in some countries, usually under the umbrella of a medical association, have become part of the EBMT data flow by mutual consent and are using the same central database. These national registries use their data for their own purposes, which may encompass national requirements for registration of transplants, research, demographics, etc. Where these registries exist, the responsibility of the EBMT Registry for data management may be partially devolved to them. Belonging to a national registry does in no way preclude the centre from exercising their rights as EBMT members, and they have as much access to the Registry staff and services as any other centre member.

2.6 International research organisations

Some centres that submit data to other organisations can request the EBMT to provide access to their data to these organisations, so they do not have to do double reporting. In these cases, the EBMT can set up virtual "registries" that replicate the scope of the organisation and provide access to a data manager of this organisation to access the permitted data. Such requests have to be submitted explicitly by the principal investigators of the involved centres. All centres must be members of the EBMT. A procedure document with request form is available for this purpose.

2.7 Membership

It is mandatory for a centre to provide Med-A data regularly in order to become a full member of the EBMT. Members that are transplant centres and do not report their data can only be associate members. At the end of every year the Executive Office, in collaboration with the Registry, will assess the submitted data for all centres. Centres that are full members that have not submitted transplant for the current year or the year before will be warned that they risk being demoted to associate membership if data is not received. Centres that are associate members will have their full membership restored if they have submitted data for the current year or the year before.

All members can obtain aggregate anonymised data on the whole database where neither the patient nor the centre are identifiable.

2.8   *Corporate sponsors*

Corporate members can obtain aggregate anonymised data, where neither the patient nor the centre, are identifiable as part of their contract. The number of reports they can receive is stipulated in the contract. If the sponsor wants to receive more reports than those stipulated, they need to pay a fee which will vary according to the complexity of the report. Sponsors cannot obtain outcome data. To safeguard centre anonymity, all countries with less than ten member centres appear under the label of "Other".

2.9   *Government agencies*

Registry data may be accessed by public agencies in one of two ways: (1) they can request direct access to data submitted by centres in their country. As with any other type of access, centres need to make the request to the Registry for their data to be accessed directly by these agencies. (2) National registries may collaborate with public agencies providing them with data extracted from the EBMT Registry. .

3   Types of Registry Users

3.1   *Users with single access*

The bulk of the Registry users are transplant centres and donor registries that access exclusively the data they themselves submit.

3.2   *Users with multiple access*

These are users that by the nature of their work have access to data from more than one centre and/or donor registry.

- EBMT Registry staff can access data from the whole Registry for research or administrative purposes.

- EBMT WP staff can access data from the Registry for research and study administration within the scope of the WP and the study, excepting data actively excluded by the centres. Permissions are signed either by the chair of the corresponding WP.

- National registry staff can access data from all transplant centres in their own country. Permission is granted by the centres themselves, and the request has to be made by the President of the national registry.

- Staff from selected government agencies can access data from all transplant centres in their own country. Permission is granted by the centres themselves, and the request has to be made by the head of the agency.

- Non EBMT Study coordinators can access data from those transplant centres or donor registries that have agreed to participate in selected studies. Permission is granted by the centres themselves, and the request has to be made by the principal investigator of the study as appointed by the study group.

- Corporate sponsors can access aggregate data for selected data items from the whole registry excepting data actively excluded by the centres.

4   Data flow

The EBMT has a single centralised database where all the data requested through the standard DCF (see *1.1* in this document) is stored. The data is currently entered and maintained through an internet management system (ProMISe). Each EBMT centre, EBMT WP or national registry has access to a virtual representation of their data in this database. In addition, particular study groups can also be provided with a virtual representation of specific populations of patients. Users from a centre, an EBMT WP, a national registry or a study group within an EBMT WP or across WPs can view, modify, obtain reports from and download their own data once the necessary permissions have been granted by the principal investigator of the centre, by the head of the national registry or EBMT WP, or the accepted director of the study group. In addition all centres and national registries can obtain general overviews from the complete EBMT database. Different levels of access are possible (see Appendix I in this document).

4.1   Flow into the EBMT database

All member centres must submit the minimum essential data as recorded through the MED-A form. The MED-A data is a subset of the data collected in the more detailed MED-B forms. For this reason, centres submitting MED-B forms do <u>not</u> need to submit accompanying MED-A forms. The first registration must be submitted on the day of transplant (day 0) or within a week of day 0. An update should be submitted when 100 days have elapsed from the date of transplant or cell therapy for non-transplanted patients, or when the patient dies, whichever comes first. Follow up data must be submitted for all patients from then onwards. For more information see document **Submitting data to the EBMT**

The data can reach the Registry through various channels:

a) Direct data entry by a centre. This is the preferred and most common method.

b) Direct data entry by a national registry on behalf of specific centres that submit paper DCFs to them.

Centres can enter the data directly (option *a*), or fill in the MED-A or MED-B paper forms and send it to their national registry (option *b*).

4.1.1   Data entered directly by the centre into the EBMT database

This method ensures immediate access by the EBMT and authorised users to the centre's data. This is the preferred method. Centres who use this system may be approached by the national registry –if they belong to one- or by the EBMT registry with requests for data corrections or clarifications.

4.1.2   Data submitted to a national registry

Usually national registries enter the MED-A and MED-B data sent to them. When this is not possible. Centres using this method can still use ProMISe to view and analyse their data, even if they are unable to do the data entry themselves.

4.2   Flow out of the EBMT database

All users of the EBMT Registry which have data from their centre or registry stored in it can obtain exports of their data. The EBMT Registry in itself does not feed into any other database. It has exported data to the CIBMTR in the past and may export data to other organisations in the

future. Following the necessary request from centres, the EBMT Registry can also export data to study groups.

4.2.1   EBMT WP use

By far the most common use of the EBMT data is performed by the EBMT WPs undertaking retrospective or prospective clinical and scientific studies. These studies are always published in peer reviewed journals. Please consult the **Guidelines for the Conduct of Registry Studies using the EBMT Registry Database** for a more detailed explanation of this use.

4.2.2   Exports performed by other users

All centres can use their own data for their own purposes. They can perform statistics on line or download their data onto their computer if they need to perform more sophisticated analyses. If forwarding data by e-mail, identifiable data must be excluded or password-protected. Any centre must abide by European Union (EU) data protection laws when downloading or viewing data, even if the data originated at the centre itself.

All national registries can use the data submitted by the centres belonging to that national registry. The rules by which these centres allow the national registries to use their data is agreed between each national registry and their respective centres. The EBMT Registry Central Office is only involved in making sure that the electronic permissions granted respect the wishes of the centres.

The study groups that exist within the EBMT Registry can use the data submitted for that purpose. The EBMT Registry Central Office is only involved in making sure that the electronic permissions granted respect the wishes of the centres.

5   Data protection and data security

5.1   Data protection legislation

The EU has produced a directive that includes regulations regarding data protection and the individual's right to privacy. This directive has become law in the EU member countries. While many other countries outside the EU have similar laws. It is the responsibility of the individual

centres or donor registries submitting data to the EBMT to make certain that the respective national laws are followed before submitting the data. It is the responsibility of the EBMT to ensure that centres and donor registries are aware of this. The EBMT requests that all centres outside the EU sign an EU Regulations Statement declaring they will follow EU regulations regarding data safety. If a centre fails to provide the EBMT with this declaration, the data can be kept, but that centre cannot be allowed access to the Registry through ProMISe, not even for its own data. It is the EBMT's legal responsibility to ensure that no access is given to centres which have failed to provide this declaration.

As of 2006 this statement is included in the forms used to request access to the EBMT Registry **DATA ENTRY APPLICATION FORM** and **DATA DOWNLOAD APPLICATION FORM**. As of 2007, this statement is also included in the EBMT membership application form, so institutions applying for membership after this date, whether inside or outside the EU/EEA, have to sign the statement in order to become members.

The EU regulations also cover the transfer of data to countries outside the EU or the European Economic Area (EEA). Within the context of the EBMT Registry, this can happen in three situations:

a)   When an EBMT WP is located outside the EU/EEA.

b)   When an investigator doing analysis on EBMT data is located outside the EU/EEA

c)   When data is transferred according to the centre's instructions to a registry collaborating with the EBMT which is outside the EU/EEA.

5.2   Database registration

As the Registry Office is located in London, the database has been registered with the Information Commissioner's Office in the United Kingdom.

5.3   Informed consent

Following the Data Protection directive, and to ensure the maximum accordance with the law of all EU/EEA nations, all individuals residing in EU member countries must give informed consent for their personal data to be entered into EBMT type registries.

The EBMT has members which do not belong to the EU/EEA countries and may submit data –for research purposes- to groups or individuals outside the EU/EEA. To cover these issues and ensure the legality of all procedures relating to the flow of research data. All centres inside and

outside the EU must obtain informed consent from their patients and/or donors before the data can be submitted to the EBMT. This informed consent must explicitly state that the data is to be kept in an "international" database and can be exported to a non-EU/EEA country. This is to avoid misunderstandings pertaining to the data being kept in a national database or even in an EU database. It is the legal responsibility of the member institution to ensure this is the case for all data submitted to the EBMT.

In the unlikely event that a subject withdraws consent after their data has been submitted, the EBMT will remove from the database all personal identifiers, including UPN, date of birth and initials, and the date of diagnosis will be reverted to "unknown". The log entries relating to the storage of these items will be deleted.

5.4   Data security implemented on site

Users must abide by all their local and national rules regarding data protection and confidentiality.

EBMT staff can only download pseudonymous data within the safe EBMT office environment. Downloading or transferring EBMT data containing personal identifiers on to personal or home computers is not allowed. If the data is downloaded for backup purposes it should be done directly onto a system recognised to be safe (locked, encrypted, etc.).

Data can be sent outside of an EBMT office for statistical analysis by EBMT approved statisticians within the context of an EBMT approved study. If the data is to be sent outside of an EBMT office or remain in a personal computer for statistical analyses, all personal items whether of the patient or of the centre (names or initials, hospital numbers, date of birth, all the fields indicating the centre where the transplant took place, contact person, etc.) should be removed and records identified solely by the SQL server autonumber field(s). The CIC part of the EBMT Unique Identification Code must also be removed since it provides information as to the transplant centre. If the transplant centre is to be a covariate in the analysis, a new field should be used by which the data can still be assigned to one centre, but which will not reveal the identity of that centre.

Centre data can also be sent outside of an EBMT office when a request has been made by the centre to the EBMT Registry to do so on their behalf. In this case, the centre making the request is responsible for ensuring that the recipient will abide by the data confidentiality rules. The EBMT retains the right to refuse to forward data if there is a perceived risk to data confidentiality by doing so.

5.5   Individual access

All individuals must submit an Access request form for internet access to the data. Accepted signatories are:

- Principal investigator of a transplant centre (centre's data only) or donor registry (donor registry's data only)

- Working Party chair (for access to data within the remit of that WP)

- The President of the EBMT (for data within the remit of an EBMT Committee)

- Director of an institution or study group with which we have a partnership. In this case, the partner must also submit a signed form from every centre involved granting access of their data to that institution or study group.

- Registry head for EBMT Registry staff

Individuals who by the nature of their work have direct access to the EBMT Registry databases (IT system/server managers) have no access rights to the data and would be in breach of contract if they manipulate it.

Appendix I – Remote access for centres

The EBMT Registry is accessed through ProMISe. In this context, ProMISe acts as an internet access system. It is free for all EBMT members and the only software it requires is a recent version of Internet Explorer. Users of ProMISe can access their own data in which case they can request permission to do any of the following:

- data entry *

- lists of patient data *

- data download *

- tables with aggregated data (frequencies and cross tabulations)

The functions with marked with * are restricted since they may include identification of the patients. This type of access can only be requested by the principal investigator (PI) of a centre for a set of nominated individuals. The request must be done in writing to the Central Registry Office and signed by the users and overall by the PI. Overall signatures of other members of the team, even if they are the heads of their respective teams (Paediatric, Adults, etc.) will not be accepted. E-mail requests are not accepted. The access provided is personal and cannot be transferred to other individuals, not even within the same centre. The Central Registry Office reserves the right to cancel access without warning if it is felt that patient confidentiality might be at risk.

The last function is available to all members. This statistical function does not allow patients or centres to be identified. Requests to receive this type of access should be made to the Central Registry Office.