EBMT

European Group for Blood and Marrow Transplantation

GUIDELINES FOR THE CONDUCT OF REGISTRY BASED STUDIES USING THE EBMT DATABASE

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1 Registry studies

One major goal when collecting data on patients whose treatment includes haematopoietic stem cell transplantation is to make it possible to perform studies. During the last 30 years many such studies have been run and published in major journals through the work of a large number of EBMT investigators. The key structure for the performance of registry studies are the EBMT Working parties (WPs). However, the EBMT structure and the structure of data collection from EBMT centres have become increasingly complex and EBMT member centres are under pressure to submit data, which is always complex and sometimes bulky. It is essential that EBMT WPs follow certain rules when preparing registry studies to ensure that centres are not overburdened by continuous and overlapping requests. At the same time, there is a need to utilise the EBMT resources and the resources from the contributing transplant centres in the most efficient way. The aim of this document is to present guidelines on how such studies should be performed to further improve the way in which registry studies are designed, carried out, analysed and reported.

2 An EBMT study

An EBMT registry study has to be initiated by an EBMT member and approved by at least one EBMT WP. This person will be responsible for the design, collection, cleaning and analyses of the data and its subsequent publication. If more than one WP is involved, it is the responsibility of the chairperson of the proposing WP to inform the chairperson of those other WPs involved in the proposed study.

Recently, the EBMT has created a series of committees (Cell Therapy, Cord Blood, etc.) which also have an interest in study data. The heads of these committees should be consulted if the study being proposed overlaps with their remit.

If an EBMT study originates outside of a WP or committee, the Registry Head can advise on which WP chairpersons should be contacted for approval of the study or, if necessary, forward the request to the EBMT Board.

3 Types of Registry studies

There are two types of studies which can be performed using the infrastructure of the Registry:

3.1 Retrospective

A retrospective study uses information on events that have taken place in the past. In most cases some or most of the data has already been gathered and stored in the registry. However and also in most cases, new data, but always on past events, may have to be requested.

3.1.1 Data collection

All data collected should be aimed to be stored in the Registry where possible (see below).

3.2 Prospective

A prospective study is initiated before the events which will constitute the end points of the study have taken place. Within this category there are two types of studies which need to be clearly differentiated:

3.2.1 Clinical trials

If the protocol of a prospective study makes requirements that will affect the management of the patient, whether in terms of the treatment itself or the investigations required to obtain the necessary data, the study forms part of what is called "Prospective Clinical Trials". Clinical trials are complex to set up and carry with them a series of legal requirements that require expert management.

3.2.1.1 EBMT sponsorship

All clinical trials must have a named sponsor which takes on legal responsibility. All clinical trials to be sponsored by the EBMT must be approved by the EBMT before they can be initiated and the necessary documentation and signatures must be in place.

All investigators wishing to conduct a clinical trial within the EBMT should refer themselves to the Clinical Trials group for information and support.

3.2.1.2 Data collection

An important difference for the EBMT is that the data collected during the running of a clinical trial must only be stored in the clinical trials database, although routine MED-AB can and should still be stored in the Registry database. In some cases, fields that may reveal the trial treatment should be left empty until the trial has closed. Advice should be sought from the Registry Office in these cases.

3.2.2 Non interventional prospective studies

Non interventional prospective studies are prospective studies which are set up to investigate events that will take place after the study has been initiated. The main and very important difference between a clinical trial and a non interventional prospective study is that the data collection or patient-participation in the non interventional study does not interfere with the choice of treatment, sample collection, procedures, and the treatment itself, which should entirely follow standard hospital practices.

Typically a non interventional prospective study behaves like a "fly on the wall" and will aim to collect information on how different centres deal with the same problem or type of patient. A non interventional prospective protocol cannot in any way set up conditions modifying either the treatment of the patient or the number or type of investigations the patient needs to be subjected to. It excludes the possibility of determining which treatment protocol should be used, randomisation or other types of patient allocation to a specific treatment, specified sample collection schedules, or collection of additional samples not included in the centre's routine procedures.

If there is the intention of collecting additional data through patient questionnaires or scheduled sample collection which are outside the normal routine of the centre, the protocol should be referred to the Clinical Trials group for advice.

Sometimes it is difficult to judge whether a prospective study is truly non interventional. This is a crucial distinction given the regulatory requirements of interventional studies. An error in making the assumption of non intervention can have a negative impact on the EBMT and it is advisable that protocols for planned non interventional studies are seen by an independent reviewer. For that reason and until further notice all protocols should be sent to Prof. Per Ljungman and Dr. Carmen Ruiz de Elvira as soon as possible after WP approval and before any implementation is initiated.

3.2.2.1 Non interventional prospective studies *versus* retrospective studies

The main advantage of a prospective study is that the selection of patients is done *a priori*, following a certain eligibility criteria, with the potential to follow them until the end of the study. With retrospective studies, the investigator cannot assess the selection bias because s/he does not know which patients will be missing from his/her study (lost to follow up, not registered, etc.). S/he only knows of the patients that are present at the moment in which the study is initiated. With a prospective non interventional study the bias due to

patient selection by unknown circumstances may not be completely prevented, but because the characteristics of all patients participating in the study are known from the beginning, the investigator will know which type of patients have been lost to the study or have poor data and will have a better idea of how inclusive the conclusions of the study can be.

In addition, as the data are collected in real time, it is possible to collect additional data (data not in the MED A or B forms) without urging the participating centres to go back to their files.

3.2.2.2 Non interventional prospective studies *versus* clinical trials

Non interventional prospective studies cannot be compared to clinical trials and cannot be used as a substitute for them. The aims are completely different since clinical trials aim at testing or comparing one or more treatments or other procedures in a controlled environment, while non interventional prospective studies can only control the selected population while any other procedures must follow the routine of the participating centres (non-interventional).

3.2.2.3 Data collection in non interventional prospective studies

Although by definition, prospective studies will always collect data in the future, they may also use data that has already been gathered and is stored in the registry. Whether this is true or not, if all or part of the data collected forms part of the Med-B set of items, these data must be stored in the Registry database.

4 Procedures for Registry studies

It is the responsibility of the EBMT Study coordinators to ensure that the correct EBMT procedures for data management are followed. The ultimate responsibility will lie with the head of the WP. It is advisable that all proposed studies are clearly listed under the WP web pages.

4.1 Initiator

Any active member of the EBMT can initiate a study. An active member is any investigator belonging to a centre that submits data to the EBMT. Usually the investigator will belong to a WP running the study. If this is not obvious and an investigator wants to use the EBMT database or the EBMT research infrastructure, the request will be forwarded to the Head of the Registry. The Head of the Registry will then suggest a WP that will have the

main responsibility for the study and forward the proposal to the WP chairperson for approval. The choice of WP will depend on the study population and its main objectives. If the choice is not clear, the Head of the Registry will consult the Board.

4.2 Concept

Once a WP has been identified, the investigator should approach the head of that WP with a brief description or concept of the study. This concept should contain a brief outline: objectives, eligibility, endpoints, number of patients, an estimate of the duration of the data collection period, an estimate of the duration of the enrolment period if the study is prospective, and budget availability, if applicable.

The WP should verify that a similar study is not being conducted already, discuss its scientific validity, consider the availability of resources necessary to run it and either reject or accept the concept. If the study is accepted, the investigator will be asked to submit the final protocol. At this point the study should be given a unique study number within the responsible WP.

4.2.1 Inter WP studies

Once the concept has been accepted by the WP chair and if the population of the study can be considered to be the remit of more than one WP or Committee, the investigators need to approach the heads of those groups and request their collaboration. Once all permissions are in place, the name, number, principal investigators, contact names for all WPs or committees involved, and the name of the study coordinator in charge of the data management need to be registered with the Registry Office.

The Registry Office keeps an "Inter WP Study" file which will be distributed regularly to the Board. This should ensure that information is widely distributed to avoid similar studies being performed by more than one WP and the Clinical Trials group.

4.3 Study protocol

Studies should not be initiated until a detailed protocol has been written, submitted to, and approved by the WP. Once approved, the protocol should not be changed without informing the participating centres. The protocol should include the following points:

4.3.1 Population

The characteristics of the population should be described unambiguously: diagnosis, age, disease characteristics, transplant specifics, period, gender, etc. For example, *female patients aged between 10 and 17 at time of transplant, receiving an allogeneic transplant between 1985 and 1990 for a non-malignant disease, and surviving a minimum of 10 years from date of transplant.*

4.3.2 Objective

The objectives of the study and its main end points (overall survival, late effects, development of complications, etc.) should be listed and defined statistically. For example, the aim of the study could be *the effects on reproductive capability for the above population, with the main end point being the frequency of live births at a certain point in time*.

4.3.3 Variables

The protocol should be accompanied by a list of variables (items, "database fields") that are essential for the study to be completed. This point is very important and should be thought out carefully. Given the characteristics of registry data a balance needs to be reached regarding the size of the population that will be available and the degree of completeness that can be achieved for each piece of data. Variables should be divided between MED-B variables (fields already present in the EBMT database) and MED-C variables (variables which will need addition of fields to the database or which may need to be stored separately).

4.3.4 Participants

For some studies, either for convenience or for other reasons, it may be advisable to restrict the number of participating centres. If this is the case, those centres should be listed at this point, either nominally or by characteristics. For example, *all centres that perform more than 10 allografts per year for non-malignant diseases.*

In some cases, the participants cannot be known because the study is based on information that has not been stored in the Registry. An example would be a small case series of rare complications where the patients are first identified by a question to the centre, using a questionnaire thereafter to collect the necessary data. In this case, the protocol rather than

the centre criteria should indicate how the participants for the first question to the centres will be selected.

4.3.4.1 Centre eligibility for non interventional prospective studies

It is advisable that the protocol for non interventional prospective studies has a paragraph on centre eligibility. The eligibility criteria should ask the centre to confirm that the patient management, including all the investigations deemed necessary to collect data for the study, form part of the centre's routine. Centres that can only participate in the study by changing their patient management must be excluded.

4.3.5 Ethical committee approval

For a registry based study, ethical approval is generally not necessary but in some cases ethical approval may be needed depending on country and on the design of the individual study. It is beyond the possibility of the EBMT to have expert knowledge about the regulations in each country. It is therefore the responsibility of the WP chair to ascertain that investigators are aware that a registry based study might require ethical approval and that the responsibility rests with the local investigator. It is therefore advisable that the protocol includes a section making the hospitals aware that they may have to apply for ethical approval under their own rules. One option could be to apply at one major centre and use that centre's approval for the entire study.

If sensitive information is being analysed (results of DNA analyses, for example), ethical committee application is strongly recommended and it will be obligatory in some countries.

4.3.6 Patient consent

For patient data to be collected by the EBMT, patient consent must have been obtained. All EBMT members submitting data to the Registry must have a procedure for obtaining patient consent for this purpose. It is highly likely that this consent is sufficient to cover most cases of registry based studies. However, because this consent may be worded in different ways in different centres, it is advisable that the protocol includes a section making the hospitals aware that they need to check whether they would need additional patient consent to forward the necessary data.

4.3.7 Time frame

A time frame for the conduct of the study should be included in the protocol, indicating when the data collection will start, when it will end and the approximate date for the publication of the results. This is particularly important for the observational studies, for which the number of patients to be recruited and the period of recruitment must be indicated.

4.3.8 Statistics

A description of the statistical techniques which will be used to analyse the data should be given (see the "Statistical guidelines" document and 6.0 below). This should include grouping of variable codes, if applicable, and a clear explanation on how missing values will be dealt with. A study statistician should be appointed at this point.

4.3.9 Authors

The authorship of the projected publication must follow the published EBMT guidelines (see below). The study protocol should list authors such as the promoter of the study, the statistician, pathologist, or any other investigator whose authorship will not be dependent on the number of patients provided for the study.

4.4 Preliminary analysis

Although each WP may have different ways of dealing with studies, it is advisable that a description of the population as it already exists in the EBMT database be produced as a first step. An important question to consider before a study is initiated is to document the completeness of the MED-B variables to be asked for. This is helpful to obtain an idea of the feasibility of the study, the likely statistical power of the investigation, and, in the case of a retrospective study, the amount of work necessary to fill in the missing data.

5 Administration

5.1 Staffing

A study coordinator and statistician should be allocated to the study. The need for staff time should be calculated early in the preparation of the study. If the WPs or Committees

involved do not have resources to cover the study, any additional staffing requirements should be requested through EBMT standard procedures and no staff can be recruited without central approval. It must be noted that non interventional prospective studies will be more labour intensive during the data collection period, but may need less work regarding the cleaning of the data.

5.2 Documentation

The study coordinator and statistician will collaborate with the principal investigator to develop the background and summary of the study, inclusion criteria (exclusion criteria), registration forms, letter of introduction, data collection forms (MED C, if necessary) and patient informed consent forms. It is important that the latter be mentioned in the introduction letter, giving the centre the possibility of making a decision as to whether it would be required according to each centre's procedures.

5.3 Budget

A study can be financed either internally through the WP budget allocated by the EBMT board or through external funding. The costs should be calculated early on and should be ready before the protocol is finalised.

A budget should at a minimum consider the following items:

- *Project management/study coordination (investigator meetings, conference calls)*
- *Central data management*
- *A per patient fee (if applicable), with an estimation of the expected number of patients*
- *Costs for quality assurance audit and overhead (10%).*
- *Statistics*

5.3.1 External funding

EBMT procedures must be followed if external funding is sought. The investigator should refer to the EBMT Treasurer for advice.

5.4 Insurance

Additional insurance is not needed for a non interventional study. If in doubt, the investigator should turn to the Clinical Trials group for advice.

6 Data collection

Requesting data from centres should aim at obtaining the most accurate data in the shortest possible time and with the least possible disruption to the activities of the centre providing the data. For this reason it is important that the protocol is clear and unambiguous regarding the patient population, that the number of data items requested is small, and that centres are not requested to provide data which they have already provided in the past. The Registry, in collaboration with national registries and EBMT study coordinators, has set up a series of rules and guidelines which are described below and which should be followed by all investigators.

6.1 Data collection and integrated National Registries

A large percentage of the data collected in the EBMT Registry is done so through the help of National Registries which have integrated themselves within the EBMT framework.

National registries are comfortable with the EBMT approaching centres directly but would like to be kept informed of the studies that their centres are requested to participate in.

6.2 Centre availability

Most studies will require extra data to be collected, sometimes prospectively and sometimes retrospectively. The study coordinator will isolate those centres that are eligible for the study (are known to contain the study population) and may be interested to participate and will approach them either directly.

In some cases centre eligibility cannot be ascertained before approaching the centre. This happens if the study aims to study patients which have been or will be submitted to certain procedures, or if the study population includes patients with rare diseases which may be registered in the Registry under a more generic disease category. Centre eligibility will then need to be ascertained at the same time as centre availability.

All centres need to be approached in the first instance with a copy of the protocol and a "Study page" or "Centre Registration form". This should include:

- the name and CIC of the centre
- WP or Committee responsible for the study
- the name of the study

- population to be studied / criteria for patient eligibility
- if applicable, centre eligibility by including a question on whether the centre manages the population to be studied
- the likely deadline for submission of the data
- the question as to whether they are willing to participate in the study either by
    - filling in additional information for retrospective studies
    - by recruiting patients into a non interventional prospective study
- request for contact details of the centre's coordinator for this study
- request for signature and dating of the form by the centre's principal investigator
- contact details of WP or Committee study coordinator to whom Study page or Registration form should be returned

In all cases where the centre belongs to a National Registry a copy of the protocol and the "Study page" or "Registration form" described above should always be forwarded to the national registries

The centre should return the "Study page" with the answer by fax, e-mail or post. Centres who respond negatively to this request should not be approached again. At the end of this document you can find a template for this type of document, taken from an original provided by the ALWP.

6.3 Forms for data collection

It is highly recommended that the preparation of these forms be done with the direct input of a study coordinator who is familiar with the EBMT database.

If variables are not yet present in the EBMT database, every attempt should be made to keep these new items to a minimum. A list of these items should be sent to the Registry Office to verify that these fields indeed do not exist, since the investigator may be unaware of fields which are present in the database but used only for a particular disease. If the items are not present, a MED-C form specific to the study can be designed. This form should not include any of the variables already included in the existing MED-B forms, and should try to follow its style and format. It is advisable to request the advice of the Registry Office, which

can check whether similar forms have been prepared by other WPs in the past, advice on how best to achieve uniformity and check that there is no overlap with existing forms. To allow the Registry Office to perform this role it is necessary this office receive copies of all study forms. This will also help in transferring MED-C variables to MED-B forms if this request is made in the future. If a MED-C form is unnecessary, the existing MED-B forms should be used with minimum modification. It has to be understood that the time consumed in data entry is proportional to the amount of changes done to the Med-B Forms.

6.4 Existing data

In most cases, retrospective studies will be dependent on existing data even if it is only for minimum registration or transplant details. This may also be the case for some observational studies if the events to be studied were to occur after transplant. In all cases, the investigators have to be aware of how to deal with existing data.

Data which has already been submitted should never be requested again. For this reason it is important that study coordinators have a clear understanding of the backlog of data waiting to be entered. It is insufficient to ask the centres to "ignore the request if data has been sent recently". This only adds to the confusion and increases the workload for the centre and for the EBMT, especially when it is discovered months later that the submitted data still has missing information and therefore a further request may need to be made.

The registrations needed for the analysis should be identified and the backlog for these registrations should be dealt with before requesting any more data.

Once all the backlog data has been entered, the existing data should be downloaded from the EBMT database and processed into a format that will allow centres to see clearly which items are missing and are, therefore, to be submitted. This only needs to be done for those centres that do not enter data directly into the EBMT database. More details on how best to approach centres depending on whether or not they do their own data entry will be given below.

6.5 Requesting data

Data should be requested from centres that have responded positively to the availability request (see above)

6.5.1 Requesting data from centres not performing data entry directly into the EBMT database

Regardless of the organisation in charge of sending the data collection request, this should be done in the following way: The centre should receive the data collection forms or an Excel version of it. If applicable, these forms should be filled with the data already available in the EBMT database. The data collection forms can be sent electronically, by fax to a secure number or by post. Electronic submission must always be done with password protected files.

If missing data is requested, the centre should be given a reasonable deadline to complete it. After completion, the centre should be asked to return the forms by any of the means above to the EBMT.

If the data is requested prospectively, the centre should be in possession of a clear schedule of when forms are due. It would be advisable that the study coordinator takes on the responsibility of warning the centres when forms are due or overdue. This is important for non interventional prospective studies since otherwise the advantages of prospectively collecting data would disappear.

6.5.2 Requesting data from centres performing data entry directly into the EBMT database

Regardless of the organisation in charge of sending the data collection request, this should be done in the following way:

6.5.2.1 Retrospective data

The centre should be provided with a list of the registrations (UICs) and asked to fill in the relevant MED-B through ProMISe. If a MED-C form is involved, this should be sent, filled with the necessary data to identify each registration (UIC, UPN, date of birth, date of transplant, etc.) already available in the EBMT database. The request to fill in the MED-B form, and the MED-C forms can be sent electronically, by fax to a secure number or by post. Electronic submission must always be done with password protected files. The centre should be given a reasonable deadline to complete it. After completion, the centre should return the MED-C form, by any of the means above to the EBMT, informing them at the same time that the MED-B data has already been entered. If there is no MED-C the centre should simply

inform the EBMT when the data has been fully entered. Electronic submission must always be done with password protected files.

6.5.2.2 Prospective data

Centres should be asked to enter all prospective data if the fields are available in the Registry. If the non interventional prospective study requires the registration of new patients and/or transplants, the centre should register these patients/transplants following the standard procedures and add the necessary data as required by the observational study protocol.

If a MED-C form is involved and the patient is already registered, this should be sent to the centre, filled with the necessary data to identify each registration (UIC, UPN, date of birth, date of transplant, etc.) already available in the EBMT database. If the Med-C will refer to non existent registrations, the centre should receive an empty Med-C form which they can reproduce for each new registration.

The request to fill in the MED-B form and the MED-C forms can be sent electronically, by fax to a secure number or by post. Electronic submission must always be done with password protected files if the documents contain patient data.

The centre should have a clear schedule for when these forms should be filled in and submitted. Submission can be done by any of the means above, informing the EBMT at the same time that the MED-B data has already been entered.

Electronic submission of Med-C data must always be done with password protected files.

6.6 Entering data

All MED-B data must be entered into the EBMT database *via* ProMISe. There are no exceptions to this rule. Keeping MED-B data outside the EBMT database in local databases or other types of files is not acceptable and it will not be uploaded into the EBMT database if this rule is not adhered to.

Regarding data that cannot currently be collected in the EBMT database due to absence of appropriate fields i.e. the MED-C form, a list of these variables should be sent to the Registry Office. Depending on the number and type of fields, these variables may be implemented within a reasonable period of time. If they cannot be implemented, advice can

be sought on how to deal with these variables. On request, the Registry Office can create a study project encompassing the study population within the EBMT database and provide data entry and statistical access to those individuals dealing with this study as requested. Note that adding specific navigation for studies cannot be done. For this reason, it is advisable that all study forms dealing with Med-B items follow as much as possible the format of the existing Med-B forms.

Data entry should be performed by the centres or by the EBMT. The same applies for non interventional prospective studies. (Any additional data that is not part of MED-B can be mailed to the relevant Study Coordinators).

Occasionally, other members of the WP or Committee may want to chase the data themselves, or even do the data entry. If this is the case they should:

a) Consult the best way of doing this with their study coordinator or with the Registry Office. The rules listed above on requesting data must be followed.

b) Agree with the responsible EBMT data managers/study coordinators on the allocation of responsibilities for data entry.

c) send a ProMISe data access request form to the Registry Office, signed by the head of the WP indicating what type of access they need (download only or data entry).

d) Ensure the data protection laws of the EU will be implemented if these members are located outside the EU.

IMPORTANT NOTE:
Data entry should not be done by individuals who have not been properly trained.

7 Procedures for statistical analysis of Registry studies.

The EBMT has published guidelines on how statistical analysis should be performed (Bone Marrow Transplantation, **48**: S1-S37, 2013). In all proposals for Registry studies, a plan for the statistical analysis to be performed needs to be included. With the exception of studies for which very simple statistical analyses are intended, it is strongly recommended that an EBMT statistician perform or at least supervise the analyses. If the analysis will not be performed by an EBMT approved statistician, it is advisable that the analysis plan, as detailed in the protocol, is reviewed and approved by an EBMT statistician before the analysis is done. This plan shall include the intended methodology in enough detail so that it

can be assessed. No study should be published in the name of the EBMT unless such a review has been performed.

8 Authorship and acknowledgement guidelines

The EBMT has issued authorship guidelines which are incorporated into the Operational Manual under the title Authorship guidelines for EBMT publications. These guidelines should be followed on publication of the Registry study.

Several journals now require listings of all WP-members as an appendix to submitted papers. It may be impossible to include investigators from all participating centres in an appendix to submitted papers. One recommended procedure is to list all members that regularly participate in WP-activities in such a list. It is the responsibility of the WP chairperson to collate such a list.

9 Requesting data from centres in countries with national registries.

National registries have agreed that during the course of the studies all contact can be made directly between the EBMT and their corresponding centres, however copies of the study protocol and "Study page" or "Registration form" should be forwarded to the national registries before centres are contacted together with a list of those centres. These national registries are willing to help the EBMT with contact information regarding their centres if so requested by the EBMT.

Centres should either send data directly to the EBMT or, if entering it directly into the EBMT database, contact the EBMT directly once they have finished with data entry. This is true for both retrospective and prospective studies.

10 Step by step procedure

10.1 First step: requesting participation

10.1.1 Documents needed

a) A "Study page" or "Registration Form" requesting participation form (see 10.4 below)
b) A cover letter with an explanation of the study
c) The study protocol or synopsis

d) The number of patients likely to be involved in this centre. If the patients are known, it would be helpful to send a list of the patients. This list must either be anonymised (only UICs) or it must be password protected.
e) Give a deadline (recommended deadline no more than 3 to 4 weeks, see figure below)

10.1.2 Sending documents

a) **To all centres:** Send e-mail to the Principal Investigator (PI) asking the centre to participate in the study. If you know who the physician likely to participate in the centre is and it is not the PI, you can e-mail him/her directly, but the e-mail must always be copied to the PI. The e-mail should also be always copied to the data manager(s) of the centre.

To national registries: Send a copy of the protocol with an indication that the centres will be contacted about this study.

10.1.3 Following up participation request

a) If the mail bounces, send it to the next physician in the on-line membership list. Alternatively, phone the centre and request a correct e-mail address. If you do the latter, and there is a national registry, contact the national registry first since they may have a more updated list of contact numbers and addresses.
b) If there is no reply, repeat the request at least twice. You can:
    a. send the request to other physicians
    b. the WP investigator in charge of the study can contact directly (phone, e-mail, face to face meeting, etc.) the centre physician who is most likely to be interested in the study
c) If the centre answers negatively, stop
d) If the centre answers positively, proceed with requesting the data

10.2 Second step: requesting data

10.2.1 Sending data request

a) **For all centres**: Mail the contact person indicated in the "participation form" with:

10.2.1.1 Retrospective data, including data needed for non interventional prospective studies

a. The data to be completed in Word or Excel format
b. A deadline (recommended deadline no more than 10 to 12 weeks, see figure in 10.5.1)

10.2.1.2 Prospective data

For prospective data, requests should be sent directly to the centres.

a. The forms to be submitted prospectively with the corresponding schedule
b. A deadline for each of the forms (see figure in 10.5.2)

10.2.2 Following up data request

a) If there is no reply,
   - repeat the request at least twice;
   - the WP investigator or study coordinator in charge of the study can contact directly (phone, e-mail, meeting, etc.) the centre physician who has agreed to participate in the study

b) On receipt of data
   - Thank the centre directly

10.3 Study completion

Always inform the participating centres and associated national registries when the study has been submitted for publication.

10.4 Study page examples

10.4.1 Retrospective study

Emmanuelle Polge, ALWP

Excellence in science EBMT European Group for Blood and Marrow Transplantation	**EBMT XXXWP(s)**

PARTICIPATION FORM

1. Name of the study

Title

2. Centre

Centre	
Name	
CIC	
Physician in charge of the study in the centre *(If applicable, this would be the author in any publication that follows from this study. See **Authorship Guidelines for EBMT publications**)*	
Name:	
E mail :	
Data manager in charge of collecting data	
Name:	
Tel :	
E mail :	

3. Deadlines

Deadline for agreement :	
Deadline for data collection :	

4. Participation

Are you willing to fill in additional information, and to complete Med B information for the study?

☐ **YES*** ☐ **NO**

* the study specific questionnaire will be sent at reception of the completed "Participation form"

Pease reply before deadline for agreement to: Name of study coordinator
: {postal address
: {-mail address}

🖷 : {fax number}

10.4.2 Non interventional prospective study

Anja van Biezen, CMWP

[Study] CENTRE REGISTRATION

Study

[Study Title]

Centre eligibility criteria *(examples)*:

Do you routinely do [procedure] for [diagnosis] in [population]? ☐ Yes
Is administration of [drug] and [drug] part of your standard treatment for [diagnosis]? ☐ Yes
Is [type] HSCT a standard option for [diagnosis] in your centre? ☐ Yes

Do you perform follow ups routinely every [number] months after the [type] HSCT? ☐ Yes
You must answer Yes to all questions in order to participate in this study.

Centre

EBMT Centre Identification Code (CIC) .....

Centre Address .....

.....

Physician in charge of the study in the centre .....
*(If applicable, this would be the author in any publication that follows from this study. See **Authorship Guidelines for EBMT publications**)*

Email address .....

Does your centre want to participate in this non-interventional prospective study?

☐ No reason:……

☐ Yes

How many patients do you expect to include in this study per year? I_I_I

Proposed Start Date: ..... - .... - ....
dd mm yyyy

IDENTIFICATION & SIGNATURE

When participating:
I agree to include all consecutive patients who agree to participate in this study and declare that the inclusion of any patient in this study will not affect the management of this patient.

..... Signature

..... Name

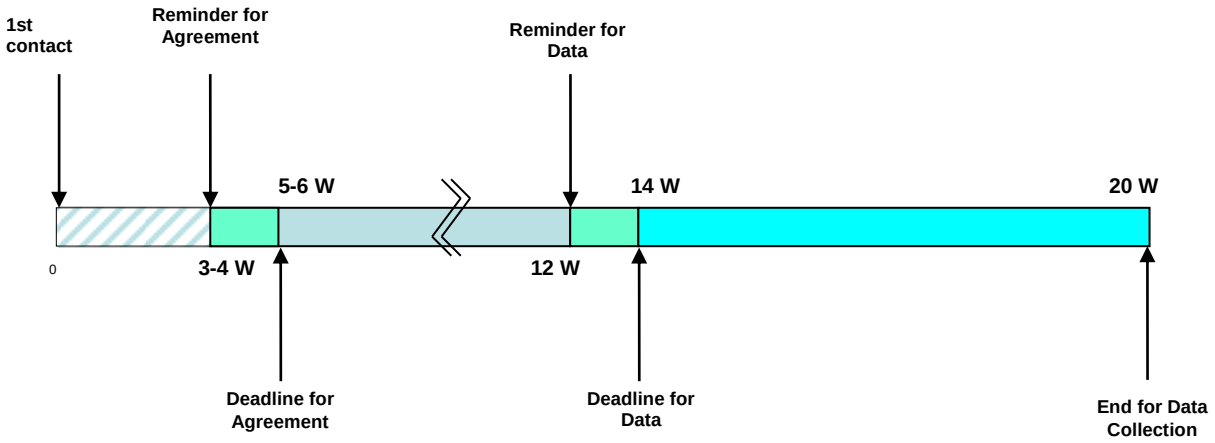
Please send the completed form to the [office] asap by using
Fax: **[fax number]** or E-mail: **[email address]**

[Full Office Contact Details]

10.5 Recommended flow and deadlines

10.5.1 Retrospective studies

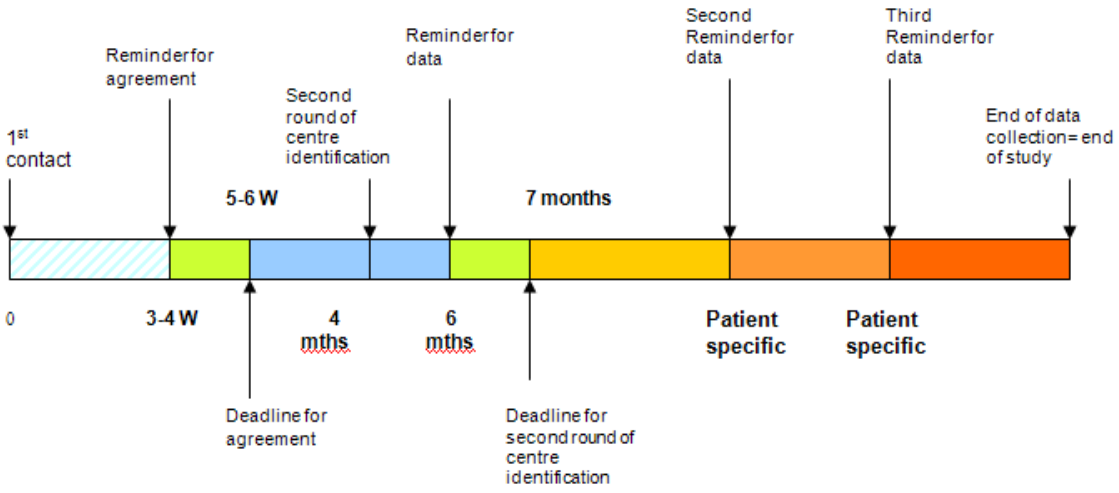
Emmanuelle Polge (ALWP), and Rosi Oneto, (SAAWP)



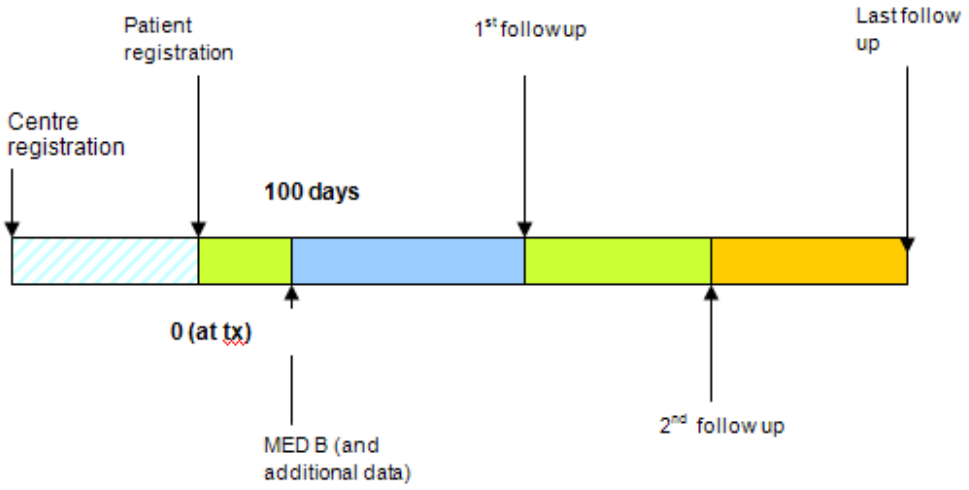
10.5.2 Non interventional prospective studies

Marijke Scholten (CMWP)

Data Flow



Data Flow per patient



11 Contributors

Anja van Biezen

Per Ljungman

Rosi Oneto

Emmanuelle Polge

Carmen Ruiz de Elvira

Marijke Scholten

Theo de Witte