

EBMT

European Group for Blood and Marrow Transplantation

CELL THERAPY FORM MANUAL

*A Guide to the completion of the EBMT
Cell Therapy Med-A Form*



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INTRODUCTION

The present document contains information on how to fill in the Cell Therapy MED-A paper form.

It is preceded by the definition of Cell therapy and information on when a new registration should be submitted to the EBMT. For general information on how to register data please visit <http://www.ebmt.org/4Registry/registry2.html>

For downloads of the Cell therapy MED-A form and instructions on where to send it please go to <http://www.ebmt.org/4Registry/registry3.html>

For information on submitting data directly to the EBMT database using ProMISe software please refer to: <http://www.ebmt.org/4Registry/registry4.html>

Updated manuals are available to download from the registry section of <http://www.ebmt.org/4Registry/registry3.html>. We are grateful for any feedback as to its content (clarity of the definitions, omissions, insufficient background or excessive verbosity, etc.). Please send all comments to the EBMT Central Registry Office to the attention of:

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CELL THERAPY REGISTRY

The Cell Therapy Registry (CTR) aims to collect data on fetal and adult stem cells, or progenitor cells used for treatment other than hematopoietic stem cell transplantation or donor lymphocyte infusion (DLI), as well as data on the clinical characteristics and outcome of the patients.

BACKGROUND

Novel cell therapies include cell preparations defined by various criteria and may be applicable to patients suffering from autoimmune, neurologic and hematologic disorder, heart disease and so on. The therapeutic potential of, for example, cytotoxic T-cells, tumor vaccines and mesenchymal stem cells (MSCs) is undergoing extensive clinical testing in areas such as cancer, tissue repair of connective tissue disorders, heart repair and immunomodulation in the setting of stem cell transplantation. In other areas, including immunological disorders such as rheumatoid arthritis and vasculitis, MSC treatment is about to enter the clinical arena.

Although these therapies may be promising and prove to be of clinical use, clinical trials are often small with a limited follow up. The detection of long-term beneficial effects, as well as late and rare side effects would require a large number of patients followed over many years.

The CTR collects data on patients treated with this novel cell therapies, to allow for analyses of their risk and benefits.

REGISTRATION OF NEW CELL THERAPY TREATMENTS

The **Cell Therapy Med-A** consists of a registration form and a very small follow up form. The Registration form should be completed and sent 3 months post cell therapy or at time of death, whichever ever occurs first. This form should be completed for a procedure in which a patient is the recipient for:

fetal or adult stem cells, and/or progenitor cells, whether the cells be hematopoietic or non-hematopoietic, not used in the setting of hematopoietic stem cell transplantation.

The centre should not fill in the **Cell Therapy Registry Med-A** form if the patient is being treated with donor lymphocyte infusions (DLI).

A centre must fill in a Cell Therapy MED-A Registration form only if the cell therapy was actually performed at that centre. The centre should not fill in the Registration form if:

- they have acted only as a referral centre
- are only involved in following the patient after therapy which has been performed elsewhere
- the harvest has been performed at this centre but the re-infusion has been performed elsewhere

For cell therapy procedures in which there is only one instance of cell infusion, it is clear that only one Cell therapy MED-A form will be filled. However, in most cases, cell therapy consists of sequential infusions. This is the recommended number of forms that should be submitted:

Description of the procedure	Number of MED-A's	Date of Cell therapy
Therapy with only one cell infusion	1	Date of infusion
Therapy with cell infusions distributed across several days, overall lasting less than 3 months and given for the same indication	1	Date of 1 st infusion
Therapy with cell infusions distributed across several days, overall lasting more than 3 months and given for the same indication	<i>n</i>	Dates of 1 st infusion at each 3 month interval
Therapy with cell infusions distributed across several days, overall lasting less than 3 months but encompassing changes in indication within that period	<i>n</i>	Date of 1 st overall infusion, date of 1st infusion after each change in indication. A change in indication resets the 3 month period.
Therapy with cell infusions distributed across several days, overall lasting more than 3 months, and encompassing changes in indication within that period	<i>n</i>	Date of 1 st overall infusion, date of 1st infusion at each 3 month interval or after each change in indication. A change in indication resets the 3 month period.

All the information contained in the Cell Therapy Med-A form must be received by the EBMT as soon as possible after 3 months have elapsed since the initial cell infusion for that period or after the patient dies, should this happen before 3 months post cell infusion. No items can be left blank unless specifically stated in the definition. If the item is marked as “unknown”, you will be asked for this information again at the time of processing the form.

The Cell Therapy - MED-A Registration and Follow up forms are subdivided in sections distributed across two columns. At the top, crossing over both columns, there is a question used to quickly identify main indication for the treatment. In the other sections the items are grouped according to various categories: centre, patient, disease, etc.

ProMISe users: If entering the data from the Cell Therapy MED-A form into the EBMT database, you should move down the left column before proceeding to the right column. Where applicable, the database field name has been added to the left of the item name in this document. If you opt to “show names” in the Actions menu in the Data Entry Editor, this field name appears on the right hand side of each item on the web page during data entry.

Cell Therapy– Med-A

First report – 3 months after 1st cell infusion of this therapy

PRIMARY INDICATION: Primary disease HSCT related

CENTRE IDENTIFICATION

EBMT Code (CIC): **CENTRE**
 Hospital: Unit:
UNIT TEAMTYPE
 Contact person..... **MEDNAME**
 Phone:.....
 Fax:.....
 e-mail:

REPORT INFORMATION

Date of this Report: - -
DAT1STRE / DATLSTRE *yyyy mm dd*

PATIENT IDENTIFICATION

Unique Patient Number or Code **UPN**
Compulsory, registrations will not be accepted without this item
 Initials: (first name(s) _family name(s))
GIVNAME / FAMNAME
 Date of Birth - - **DATPATBD**
yyyy mm dd
 Sex Male Female **PATSEX**

INDICATION FOR TREATMENT

If Primary disease: **DISMCLFD**
 Date of diagnosis - - **IDAABB**
yyyy mm dd
 Autoimmune disease, specify **VDIAGTX**
 Neurologic disorder, specify
 Heart disease, specify
 Haematologic, specify
 Other, specify
 If Haematopoietic stem cell transplant related GvHD prophylaxis
 GvHD treatment
 Prevention of rejection
 Graft enhancement
 Bone marrow failure

CELL THERAPY TREATMENT

Date of first cell infusion - - **IDAABE**
yyyy mm dd **IDAABC**
Performance score System Karnofsky
 Score: **PERFSYST** Lansky **PERFSTAT**
10 20 30 40 50 60 70 80 90 100
Status at therapy
 Chronic Acute **CHRACU**
 Acute exacerbation of chronic disease
Cell origin **CETHORIG**
 Allogeneic Autologous
Tissue cell source (check all that apply)
 Bone Marrow **VBMSC** Peripheral Blood **VPBSC**
 Cord Blood **VCBSC** Adipose **ADIPCELL**
 Endothelial cell progenitor **ENDOCELL**
 Other, specify **VOTSC VSTMSOUR**
Cell characteristic (check all that apply) **MONNCEL**
 Mononuclear cells CD34+ **CD34POS**
 Mesenchymal **MESECHYM** Unseparated bone marrow
 Other, specify **UNSEBPM**
VADOTHER VADCELLS **CELLTHNR**
Chronological no. of cell therapy for this patient (if more than 3 months apart or for a different indication)

GRAFT MANIPULATION

Ex-vivo manipulation **EXVIMANI**
 No Yes: Growth factor, specify **IDAABCCD**
EXVIGRWF Other **VPSOTHER VPOSSELO**
 Expansion **VEXPANSI**
 Unknown
In-vivo manipulation **TRTDONOR**
 In the donor **VCYTKODN VCYTOSD**
 No Yes: Growth factor, specify **GWFACTDO**
 Other
 Unknown **DONMANO DONMANOS**
 In the patient **VGRWFACT**
 No Yes: Growth factor, specify **IDAABCCD**
VSUPHTER Other
 Unknown **VOTHERT VOTHERTS**

TREATMENT

Route of infusion (check all that apply)
 Intravenous **INTRAVRT** **ARTERTT ARTERTTS**
 Locally intra-arterially, specify artery
 Locally into tissue **TISSUERT** Intraperitoneally **PERITRT**
 Intra bone **BONERT** Intrathecal **THECALRT**
 Other route **OTHERRT OTHERRTS**

Dose

Total N° of infusions **NUMBINFO**
 N° of cells infused per infusion x 10⁶/kg

Associated procedure (ie: HSCT CABG, decompression of spinal cord injury, matrix implant etc.) **PROCED**

No **PROCEDS**
 Yes: specify
 Prior to cell therapy **TIMEPROC**
 Simultaneous
 Post cell therapy
 Unknown

RESPONSE

Best clinical/biological response after cell therapy **TUMRSA2**

Complete sustained remission (CR)
 Partial sustained remission (PR)
 Remission (CR or PR) followed by relapse or progression
 Stable Progression Unknown

Laboratory response (if applicable) **LABSTAT**

Normalized
 Improvement
 Unchanged
 Worsening

Specify laboratory parameter **LABPAR**

DATE OF LAST CONTACT

Date of last follow up or death: - - **IDAABE**
yyyy mm dd

Survival Status **VPATSTAT**

Alive Dead
 Check here if patient lost to follow up

Main Cause of Death (check only one main cause) **VCAUSDTH**

Relapse or Progression (if indication: primary disease)
 HSCT related (if applicable): **DEACSBMR**
 Cell Therapy related:
 Other **DEACSBMU**
 Unknown

Cell Therapy– Med-A

Follow up report – 1 year post cell therapy and annually thereafter

PRIMARY INDICATION: Primary disease HSCT related

CENTRE IDENTIFICATION

EBMT Code (CIC): CENTRNR
 Hospital: Unit: UNIT
 TEAMTYPE
 Contact person..... MEDNAME
 Phone:.....
 Fax:.....
 e-mail:

REPORT INFORMATION

Date of this Report: - -
 D DATREP TRE / DATLSTRE yyyy mm dd

PATIENT IDENTIFICATION

Unique Patient Number or CodeUPN
Compulsory, registrations will not be accepted without this item
 Initials: (first name(s) _family name(s))
 GIVNAME / FAMNAME
 Date of Birth - - DATPATBD
 yyyy mm dd
 Sex Male Female PATSEX

DATE OF LAST CONTACT

Date of last follow up or death: - -
 IDAABE yyyy mm dd

DISEASE STATUS AT LAST CONTACT

Best clinical/biological status since last follow up VDISESTA

- Complete sustained remission (CR)
- Partial sustained remission (PR)
- Remission (CR or PR) followed by relapse or progression
- Stable Progression Unknown

PATIENT STATUS

Survival Status VPATSTAT

- Alive Dead
- Check here if patient lost to follow up

Main Cause of Death (check only one main cause) VCAUSDTH

- Relapse or Progression (if indication: primary disease)
- HSCT related (if applicable): DEACSBMR
- Cell Therapy related:
- Other DEACSBMU
- Unknown

INSTRUCTIONS

INDICAT PRIMARY INDICATION

Indicate which is the primary indication for the cell therapy treatment:

Primary disease means primary disorder as the reason for cell therapy, i.e. heart disease (angina pectoris, heart failure), multiple sclerosis, inflammatory bowel disease etc.

HSCT related means treatment (such as mesenchymal cell (MsC) infusion) used to treat a complication associated to hematopoietic stem cell transplantation (HSCT), i.e. graft-versus-host disease, graft failure etc.

CENTRNR EBMT Code (CIC)

Every transplant centre on submitting data to the EBMT receives a CIC which should be entered here. If you do not know your CIC, look it up in the correspondence you have received from the EBMT Secretary or the Registry Office. If you still cannot find it, you can search for your centre in the EBMT website at:

<http://www.ebmt.org/ebmt/members/search4b.htm>

If you are not a member of the EBMT but want to report data, contact the EBMT Registry Office to obtain a CIC before submitting the data.

This item is essential for proper registration of your data.

Hospital

Write the name in full of your hospital. Include the city and country. If you are submitting several forms in one go, you may want to omit this item in all forms but the top one. However, this cannot be done if you have not entered your CIC code (see above).

UNIT Unit

Write down the name of your Unit (i.e. Paediatric Haematology, Haematology, Oncology, BMT Unit, etc.). You may also identify your unit by its current director. It is likely, however, that the head of a unit may change in the future, so this may not be the best way to identify it.

Entering this information is particularly important if your centre has more than one unit reporting independently to the EBMT. Ensure that you always use the same name in the future.

MEDNAME Contact person

Write down the name of the person who will be responsible for updating or correcting the data contained within the MED-A forms should this be necessary.

Phone

Write down the phone number at which the contact person (defined above) is most readily available. If you are submitting several forms in one go, you may want to omit this item in all forms but the top one.

Fax

Write down the fax number at which the contact person (defined above) is most readily available. If you are submitting several forms in one go, you may want to omit this item in all forms but the top one.

E-mail

Write down the e-mail full address of the contact person, as defined above. If this person does not have a personal e-mail, write down the e-mail address of another person in the unit who would be willing to act as an intermediary. If you are submitting several forms in one go, you may want to omit this item in all forms but the top one.

DA1STRE Date of this report

This is the date the data for the patient data submitted with this form was collated or put together. If you enter the data directly from the patient notes, it is the date you are entering the data. If you fill in a paper Med-A form, it is the date you filled in the form. This date will remain unchanged regardless of how much more data you add to the patient record.

UPN Hospital unique patient number or code

Write here the number/code used by the treating centre to uniquely identify this patient. This can be the UPN (unique patient number) used by the hospital, or a code given by the cell therapy unit. **This item is compulsory.** It must be unique, by itself should suffice to identify the patient and should not be liable to change. If a patient receives a second treatment, do not assign a new number: use the same unique number for this patient when registering subsequent cell infusions.

GIVNAME Initials (first name(s) - surname(s))

Write the initial of the first name of the patient followed by the initial of the surname of the patient. In countries where it is customary to do so, you can write down the initials of the first and second surname of the patient after the initial of the first name. If the local hospital guidelines or national law do not allow initials to be provided to third parties, you can write a code which has the approval of your hospital

Make sure there is consistency in the way the identification of the patient is given so the record can always be traced even if the patient remains anonymous.

DATPATBD Date of birth

Write the date of birth of the patient. If you do not know the exact date, apply the following: If you know the month and year but not the day, use "01" as day; If you do not know the month, use "01" (January) as month. Indicate that the date is approximate if applicable.

PATSEX Sex

Indicate the gender of the patient.

INDICAT INDICATION FOR TREATMENT

If Primary disease

IDAABB Date of diagnosis

If the patient is being treated for a primary disease, unrelated to HSCT procedures, write down the date of diagnosis of the disease for which the patient is being treated.

Tick a box for the disease for which the patient is being treated.

DISMCLFD Do not tick boxes for diseases the patient may have had in the past if the procedure being reported is not meant to deal with them.

Hamematopoietic stem cell transplant related

VREASDL1 Tick a box for the HSCT related complication for which the patient is being treated.

CELL THERAPY TREATMENT**IDAABC Date of first cell infusion**

Date of first cell therapy treatment. For patients receiving cell therapy for a complication of HSCT, put date of first cell therapy treatment, not date of HSCT.

PERFSYST Performance score

KARNOFSK The Karnofsky and Lansky are standard performance scales, which can be found in Appendix I of this manual. The Karnofsky is used for adults and the Lansky is used in paediatrics.

CHRACU Status at therapy

Chronic: For example chronic heart failure, multiple sclerosis, systemic sclerosis.

Acute: Disorder treated with cell therapy soon after onset, i.e. acute heart failure after myocardial infarction, cell therapy for recent tissue injury etc.

Acute exacerbation of chronic disease: For example rapid onset worsening of inflammatory bowel disorders or multiple sclerosis.

CETHORIG **Cell origin:** Indicate whether the cells infused proceeded from the patient or from another person

Allogeneic the patient receives stem cells from another person

Autologous the patient receives his/her own stem cells back

VBMSC Tissue cell source

VPBSC, etc Tissue from which the cells were harvested, for example, bone marrow, adipose tissue, muscle.

MONNCEL Cell characteristic

MESECHYM Composition of cells used for therapy. For example, whole bone marrow encompassing several types of cells, mononuclear cells derived from bone marrow, mesenchymal stem cells etc. One or several types of cells might be used to treat the patient on a single occasion.

CELLTHNR Chronological number of cell therapy for this patient

Refers to cycle of cell therapy, when applicable, in which the 1st infusion is given more than 3 months apart or when the indication for the cell therapy has changed. If patients receive several infusions within 3 months for the same indication, this is stated under TREATMENT Dose and not here.

GRAFT MANIPULATION**EXVIMANI Ex vivo manipulation**

Refers to treatment of the harvested cells/tissue in the laboratory before infusion into the patient.

VSUPHER In vivo manipulation

Refers to treatment of cells/tissue prior to harvest from the donor -or patient if autologous cells are used – mostly used to mobilise the cells facilitating collection.

TRTDONOR In the donor: I.e. administration of growth factors (such as GCSF, GM-CSF) to the donor before cell harvest.

VGRWFACT In the patient: As above but in patient.

TREATMENT**INTRAVRT Route of infusion**

ARTERRT etc Indicate in which way were the cells administered. Several routes can be used simultaneously.

TISSUERT Locally into tissue also includes implantation of cells on matrix (i.e. cells allowed to adhere to an implant device, such as collagens, sponge, in the laboratory, where one or several such sponges are plated in the patient).

CELLTHNR Dose

Indicate the total number of infusions a patient receives within the cycle covered by the form (3 months maximum length or after a change in indication) and the average number of cells per infusion.

PROCED Associated procedure

Depending on the disease, the patient may receive other type of treatment together with the cell therapy, for example, they may receive the cells at time of coronary by-pass surgery, spinal cord decompression, etc. It is important to know whether this was the case or whether the patient was not undergoing such concurrent treatment.

TUMRSA2 RESPONSE

LABSTAT Given the different types of indications, the response parameters will vary greatly. It can include clinical, biological and/or laboratory responses. That is why it is important to indicate, as applicable, the response itself and the laboratory response, specifying the parameters measured to define the laboratory response.

Examples would include disappearance of all symptoms of graft-versus-host disease in patients treated with MSC for this disorder; improvement of heart failure in patients treated with cell therapies after myocardial infarction; or reduced inflammatory lab parameters in patients with rheumatologic disorders; etc

IDAABE DATE OF LAST CONTACT

Date of last follow up or death is the exact date the patient was last known to be alive or the date of death, if applicable.

If the patient cannot be traced (for example, left the country), put the exact date the patient was last known to be alive under Date of last follow up or death and tick the box Check here if patient lost to follow up

VCAUSDTH Main cause of death

The information on cause of death is very important. Tick only one major cause of death. Please check with your physician since this information is sometimes difficult to find in the patient's file.

- Relapse or progression
- HSCT related
- Cell therapy related

In the absence of clinical disease, a death caused by complications or infections after cell therapy is considered treatment related. If the patient has not had any HSCT, the cause of death would be considered **Cell therapy related**. However, if the patient had also had an HSCT, it may also be HSCT related. Check with your physician.

In the presence of clinical disease, if the disease is progressing, the death will be considered as **Relapse or progression**, even if there are complications or infections during the post cell therapy infusion period. However, if the disease was stable, or there had been an improvement after cell therapy, and the patient were to die of complications or infections, the death would be considered treatment related.

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Appendix I

KARNOFSKY SCALE

- 100: Normal, no complaints or evidence of disease
- 90: Able to perform normal activity; minor signs and symptoms of disease
- 80: Able to perform normal activity with effort; some signs and symptoms of disease
- 70: Cares for self, unable to perform normal activity or to do active work
- 60: Requires occasional assistance but is able to care for most of own needs
- 50: Requires considerable assistance and frequent medical care
- 40: Requires special care and assistance; disabled
- 30: Hospitalization indicated, although death not imminent; severely disabled
- 20: Hospitalization necessary; active supportive treatment required, very sick
- 10: Fatal processes progressing rapidly; moribund
- 0: Dead