2003: Gene Therapy Product

This form must be completed for all products for Gene Therapy recipients. All patients receiving a Gene Therapy product will be placed into the CRF track. For TED only reporting centers, Form 2003 will also need to be completed.

The Gene Therapy Product (2003) form is designed to capture product specific information for all infusions given to a recipient as a course of gene therapy. PBSC collected from a single mobilization event (a mobilization event is the planned administration of growth factors or systemic therapy designed to enhance stem cell collection), even when collected over several days, is considered one product.

Multiple products are collected when, for example, the donor requires another mobilization to collect a product at a later date. The collection from the second mobilization event is considered a different product and should be reported on an additional 2003 form.

For more information see **Appendix D – How To Distinguish Infusion Types** and **Appendix E – Definition of a Product**.

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please reference the retired manual section on the **Retired Forms Manuals** of the CIBMTR Forms Instruction Manual is intended to be a resource for completing the Gene Therapy Product Form.

Date	Manual Section	Add/ Remove/ Modify	Description
6/25/ 2024	2003: Gene Therapy Product	Add	Due to change in FN validation, product Processing / Manipulation blue box added above Q13: ***Product Processing / Manipulation****: This section applies only when* ***Other*** *name is reported in question 1. If a commercially available product was selected in question 1, continue with Specify the timepoint in the product preparation phase that the product was analyzed.*
12/	2003:	Add	Bone Marrow Products blue information box added above Q6: **Bone Marrow**

18/ 2023	Gene Therapy Product		**Products**: If the Gene Therapy product is mobilized from the bone marrow, select **Not done** for the questions *Peripheral blood CD34+ cell count prior to first dose of cytokine for mobilization (baseline)* and *Peripheral blood CD34+ cell count on Day 1 apheresis, just prior to start of procedure*.
10/ 29/ 2021	2003: Gene Therapy Product	Add	Version 1 of the 2003: Gene Therapy Product section of the Forms Instructions Manual released. Version 1 corresponds to revision 1 of the Form 2003.

Last modified: Jun 25, 2024

Q1 – 5: Product Identification

A Gene Therapy Product (2003) form will be completed for each product administered

Question 1: Name of Product

The name of the product reported will be auto populated from what was reported on the Pre-TED (F2400) form.

Questions 2 – 5: Specify the identifier(s) associated with this gene therapy product (check all that apply)

Indicate the identifiers (Product ID, Batch Number, or Lot Number) associated with this gene therapy product. At least one identifier should be reported. Check all that apply.

- **Gene therapy product ID:** Product IDs can be numeric or alphanumeric and are found with the product bag or shipping manifest.
- **Batch number**: Batch numbers can be numeric or alphanumeric and are available with the information that comes with the product
- **Lot number:** Lot numbers can be numeric or alphanumeric and are available with the information that comes with the product

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Last modified: Oct 23, 2023

Q6 -12: Product Collection

Multiple collections versus multiple products
The Gene Therapy Product (2003) form collects the information for a single product. PBSC cells collected from a single mobilization event (a mobilization event is a planned administration of growth factors or systemic therapy designed to enhance stem cell collection), even when collected over several days, is considered one product. Multiple products are collected when, for example, the donor requires another mobilization to collect a product at a later date. The collection from the second mobilization event is considered a different product and should be reported on an additional Gene Therapy Product (2003) form.

Bone Marrow Products
If the Gene Therapy product is mobilized from the bone marrow, select **Not done** for the questions *Peripheral blood CD34+ cell count prior to first dose of cytokine for mobilization (baseline)* and *Peripheral blood CD34+ cell count on Day 1 apheresis, just prior to start of procedure*.

Questions 6 – 7 Peripheral blood CD34+ cell count prior to first dose of cytokine for mobilization (baseline)

The recipient's peripheral blood CD34+ cell count is often determined prior to the start of mobilization as it may predict success of PBSC mobilization.

Indicate if the peripheral CD34+ cell count was performed *prior to the first dose of cytokine for mobilization (baseline)*. If **Done**, report the CD34+ cell count at baseline per microliter (uL) or cubic millimetre (mm3).

Questions 8 – 9 Peripheral blood CD34+ cell count on Day 1 apheresis, just prior to start of procedure.

Indicate if the peripheral blood CD34+ count was performed *just prior to connecting the recipient to the apheresis machine*. If **Done** report the CD34+ cell count per microliter (uL) or cubic millimetre (mm3).

When reporting this value, review the apheresis start time to ensure the CD34+ cell count was performed prior to the start of the procedure.

Question 10: Date of first collection for this mobilization

Report the first date the gene therapy cell collection was performed. If the collection event occurred over multiple days, enter the date the collection started (i.e. Day 1)

Example 1: An autologous recipient was mobilized with G-CSF and underwent a two-day PBSC collection. Since the collection and mobilization methods remained the same over the duration of the collection, this collection is considered one product. Report the collection start date as the date of product collection.

Example 2: An autologous recipient was mobilized with G-CSF and underwent a two-day PBSC collection. The collected cell counts were poor, and no further collections were attempted. One week later the recipient was re-mobilized with G-CSF and a second PBSC collection was performed. Due to the recipient having two mobilization events, this is considered two separate products. The date of first collection should be the first day of collection for the product for which the form is being completed.

Questions 11 – 12: Was more than one collection required?

If more than one day of collection was required for this mobilization event, select **Yes**, and report the total number of subsequent days of collection. Do not report days of collection for a different product as each product is reported on a separate 2003 form.

Section Updates:

Question Number	Date of Change	Add/ Remove/ Modify	Description	Reasoning (If applicable)
Q6	12/18/ 2023	Add	Bone Marrow Products blue information box added:**Bone Marrow Products**: If the Gene Therapy product is mobilized from the bone marrow, select **Not done** for the questions *Peripheral blood CD34+ cell count prior to first dose of cytokine for mobilization (baseline)* and *Peripheral blood CD34+ cell count on Day 1 apheresis, just prior to start of procedure*.	Added for clarification

Last modified: Dec 18, 2023

Q13 – 29: Product Processing / Manipulation

Product Processing / Manipulation
This section applies only when **Other** name is reported in question 1. If a commercially available product was selected in question 1, continue with *Specify the timepoint in the product preparation phase that the product was analyzed*.

Questions 13 – 16: Where was the gene therapy product manufactured / processed?

Indicate the location where the gene therapy product was manufactured / processed.

- **Cell processing laboratory at the same center as the product is being infused**: The gene therapy product was manufactured / processed at a cell processing lab associated with the same center where the product is being infused. This includes both cell processing labs located onsite and offsite.
- **Cell processing laboratory offsite**: The gene therapy product was manufactured / processed at a cell processing lab, not associated with the transplant center, such as stand-alone or privately held manufacturing / processing lab. This does not include pharmaceutical / biotech companies.
- **Pharmaceutical / biotech company**: The gene therapy product was manufactured / processed **by or on behalf of a** pharmaceutical or biotech company (see question 14 for a list of possible pharmaceutical / biotech companies). Companies may partner with other companies to perform the manufacturing / processing. If the company is not listed from the options provided, select **Other pharmaceutical / biotech company** and specify the company in question 15.
- **Other site**: If the gene product therapy was manufactured / process at a site not listed above, select this option, and specify in question 16.

Question 17: Specify the portion of the gene therapy product manipulated

Report the portion of the gene therapy product manipulated. This information may be found with the gene therapy product processing information that comes with the product . If the entire product was manipulated, select **Entire product**. If only a portion of the product was manipulated select **Portion of product**.

If the portion of the gene therapy product manipulated is not known, select **Unknown**.

Question 18: Was the manipulated product cryopreserved?

Specify Yes or No if the manipulated gene therapy product was cryopreserved prior to infusion.

Question 19: Was the unmanipulated (“back up”) portion of the product cryopreserved?

Specify **Yes** or **No** if the unmanipulated portion of the gene therapy product was cryopreserved for future use.

This question is only enabled if the portion of the gene therapy product manipulated is **Portion of the product**.

Question 20: Specify the type(s) of genetic manipulation

Specify the type(s) of gene manipulation. Check all that apply.

- **Ex vivo transduction**: Ex vivo transduction is a method of using a carrier (called a vector) to introduce genetic material into cells that are outside (ex vivo) the body. If this option is selected, continue with question 25.
- **Gene editing**: Gene editing refers to the manipulation of the genetic material by deleting, replacing, or inserting a DNA sequence. If this option is selected, continue with question 25.
- **Other genetic manipulation**: If a method of genetic manipulation was performed on the gene therapy product but is not listed above, select this option, and continue with question 29.

Questions 21 – 22: Type of vector

A vector is used to carry foreign genetic material into another cell. Specify the type of vector used in ex vivo transduction. This information may be available from a clinical study protocol or information that comes with the product. If **Other vector** is selected, specify the vector in question 22. If the type of vector is not known, select **Unknown**.

Transgenes
ABCD1 is a transgene specific for adrenoleukodystrophy. **Beta globin (wild type, T87Q, AS3), Gamma globin (G16D, other), and shRNA/siRNA to BCL11A** transgenes are specific for hemoglobinopathies.

Questions 23 – 24: Specify the transgene

A transgene is the therapeutic gene that has been transferred into the gene therapy product cells. This information may be available from a clinical study protocol or information that comes with the product. Specify the transgene used in ex vivo transduction. If **Other transgene** is selected, specify the transgene in question 24. If the type of transgene is not known, select **Unknown**.

Questions 25 – 26 : Methodology

Specify the methodology used for gene editing. This information may be available from a clinical study protocol or information that comes with the product.

- **Base editor**: a genome editing approach that uses the CRISPR (clustered regularly interspaced short palindromic repeats) system with enzymes to directly install point mutations into cellular DNA or RNA without making double-stranded DNA breaks.
- **Cas protein**: a genome editing approach that uses the CRISPR (clustered regularly interspaced short palindromic repeats) system with the Cas protein to cut DNA at the targeted site.
- **Transcription activator-like effector nucleases (TALENs)**: restriction enzymes that can be engineered to cut specific sequences of DNA.
- **Zinc finger nucleases (ZFNs)**: class of engineered DNA-binding proteins that facilitate targeted editing of the genome by creating double-strand breaks at the targeted site.

- **Other methodology**: If the method of gene editing is not listed above, select this option, and specify in question 26.
- **Unknown**: If the methodology of gene editing is not known, select this this option.

Questions 27 – 28: Specify the gene target

Specify the name of the gene targeted for editing. If **Other** is selected, specify the gene target in question 28. If the gene target is not known, select **Unknown**.

Question 29: Specify other genetic manipulation

If the method of genetic manipulation is other than ex vivo transduction or gene editing, specify the method of genetic manipulation.

Section Updates:

Question Number	Date of Change	Add/ Remove/ Modify	Description	Reasoning (If applicable)
Q13	6/25/ 2024	Add	Product Processing / Manipulation blue box added above Q13: ***Product Processing / Manipulation****: This section applies only when* ***Other*** *name is reported in question 1. If a commercially available product was selected in question 1, continue with Specify the timepoint in the product preparation phase that the product was analyzed.*	Due to change in FormsNet3 validations

Last modified: Jun 25, 2024

Q30 – 68: Product Analysis (All Products)

Reporting Multiple Instances of Product Analysis
To report multiple instances of product analysis, complete questions 30-68 by adding additional instances in FormsNet3SM

Question 30: Specify the timepoint in the product preparation phase that the product was analyzed

Report the time in the product preparation phase the product was analyzed. A maximum of three timepoints may be reported. Each timepoint can only be reported once.

- **Fresh manipulated product**: Assessment of a *fresh manipulated* product. This will usually be performed at the manufacturing / processing site
- **Prior to cryopreservation of manipulated product plus additives**: Assessment of a *fresh manipulated* product, plus additives. This will usually be performed at the manufacturing / processing site
- **Post-thaw of cryopreserved manipulated product**: Assessment of the cryopreserved, manipulated product after thawing. This will usually be performed at the transplant center prior to infusion of the product

Question 31: Date of product analysis

Report the date when the product was analyzed for each timepoint reported. **The date of product analysis is not necessarily the date of the product infusion**.

Question 32: Total volume of product plus additives

Enter the total volume of the product plus additives in the bag(s) for the reported timepoint. Report the volume in milliliters (mL).

Questions 33 – 34: CD34+ cells

Indicate if the CD34+ cells were quantified at the reported timepoint. If **Done**, report the absolute number of CD34+ cells for the specified timepoint. Do not report cells per kilogram. If the CD34+ cells were not quantified for the specific timepoint, select **Not done** and continue with question 39

CD34+ and TNC Viability
The anticipated viability will only be done on CD34+ cells; however, the TNC viability may be reported if CD34+ viability was not performed. If both the CD34+ and TNC viability were performed, report the CD34+ viability . If neither the CD34+ and TNC viability was performed, report **Not done**.

CD34+ Viability
If viability was performed on the entire product or select cells (i.e. viability was performed on both the CD34+ and CD3+ cells) and not on the CD34+ cells alone, report **Not done** for the CD34+ viability.

Questions 35 – 36: Viability of CD34+ cells

If the viability of the CD34+ cells was quantified, select **Done** and report the percentage of viable cells. If the viability was **Not done**, continue with question 39.

Select **Unknown** if there is no documentation to confirm if viability was performed.

If the laboratory assay only measures CD34+ viable cells, report the number of viable CD34+ cells in question 34, select **Done** for question 35, and report a viability of **100%** in question 36.

Questions 37 – 38: Method of testing CD34+ cell viability

Indicate the method of testing viability

- **Flow cytometry based**: 7-AAD (7-aminoactinomycin D) and propidium iodide are compounds that can stain dead cells but will not cross the membrane of living cells. Cytometric techniques are used to calculate the percentage of viable cells in a sample.
- **Trypan blue**: a technique where the dead cells become stained when in contact with the compound, but living cells remain impermeable to the dye. Cells are counted under a microscope to determine the percentage of viable cells in a sample.
- **Other method**: If the cell viability was tested using a different method, select this option and specify the method in question 38.

Questions 39 – 40: Other cell type

Indicate if an “other” cell type was quantified at the reported timepoint. If **Done**, report the total number of “other” cell types tested. The maximum number of cell types that can be reported is four. The number of cell types reported will enable the appropriate number of instances (questions 41 – 64) in FormsNet3SM.

If no “other” cell types were quantified at the reported timepoint, select **Not done** and continue with question 65.

Questions 41 – 64: Specify other cell types

For each cell type, a separate instance will be enabled. Specify the “other” cell type quantified at the reported timepoint and report the absolute number of cells. Do not report cells per kilogram.

Additionally, indicate if the viability if the “other” cells were quantified. If **Done**, report the viability percent of cells and specify the method of testing for viability. Select **Unknown** if there is no documentation to confirm if viability was performed. For commercial products, the viability will be performed at the manufacturing site and this information may or may not be reported to the transplant center.

- **Flow cytometry based**: 7-AAD (7-aminoactinomycin D) and Propidium iodide are compounds that can stain dead cells but will not cross the membrane of living cells. Cytometric techniques are used to calculate the percentage of viable cells in a sample.
- **Trypan blue**: a technique where the dead cells become stained when in contact with the compound, but living cells remain impermeable to the dye. Cells are counted under a microscope to determine the percentage of viable cells in a sample.
- **Other method**: If the cell viability was tested using a different method, select this option and specify the method.

Select **Unknown** if there is no documentation to confirm if viability was performed. For commercial products, the viability will be performed at the manufacturing site and this information may or may not be reported to the transplant center.

Vector copy number (VCN)
The VCN for the infused product is only enabled if **Ex vivo transduction** is reported as a genetic manipulation.

Questions 65 – 66: Vector copy number (VCN) in the infused product

A vector copy number (VCN) is the number of vector copies per diploid genome. This information may be available from a clinical study protocol or information that comes with the product. Indicate if the VCN of the infused product is **Known** or **Unknown**. If **Known**, report the VCN. If **Unknown**, continue with question 67.

Percentage of gene edited cells
The percentage of gene edited cells for the infused product is only enabled if **Gene editing** is reported as a genetic manipulation.

Questions 67 – 68: Percentage of gene edited cells in the infused product

When product is genetically modified by gene editing, the percentage of gene edited cells maybe be known. This information may be available from a clinical study protocol or information that comes with the product. Indicate if the percentage of gene edited cells in the infused product is **Known** or **Unknown**. If **Known**, report the percentage of gene edited cells. If **Unknown**, continue with question 69.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Last modified: Oct 23, 2023

Q69 – 75: Product Infusion

Question 69: Date of manipulated product infusion

Report the date this product was infused. If the product was infused over multiple days, report the first date of infusion.

Questions 70 – 71: Specify the route of product infusion

Report the route by which the product was infused.

- **Intravenous**: refers to the infusion into the veins. Examples include infusion via central line or via catheter.
- **Other route of infusion**: If the product was infused other than intravenously, select this option and specify in question 71. This option should be used sparingly since the only known method of infusion for gene therapy products is intravenously.

Question 72: Was the unmanipulated (“back up”) product infused?

Indicate **Yes** or **No** if the unmanipulated product was infused. If **No**, continue with the Signature Lines.

This question is only enabled if it is reported a **Portion of product** was manipulated.

*Question 73: Date of unmanipulated product infusion

Report the date the unmanipulated product was infused. If the product was infused over multiple days, report the first date of infusion.

*Questions74 – 75: Specify the route of unmanipulated product infusion

Report the route by which the product was infused.

- **Intravenous**: refers to the infusion into the veins. Examples include infusion via central line or via catheter.
- **Other route of infusion**: If the product was infused other than intravenously, select this option and specify in question 75. This option should be used sparingly since the only known method of infusion for gene therapy products is intravenously.

*Signature Lines:

The FormsNet3SM application will automatically populate the signature data fields, including name and email address of person completing the form and date upon submission of the form.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Last modified: Oct 23, 2023