2003: Gene Therapy Product

This form must be completed for all products for Gene Therapy recipients. All recipients receiving a gene therapy product will be placed into the HCT CRF track. For HCT TED only reporting centers, the Gene Therapy Product (2003) form 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**.

Links to Sections of Form:

- Q1 – 6: Product Identification
- Q7 – 15: Product Collection
- Q16 – 32: Product Processing / Manipulation
- Q33 – 71: Product Analysis (All Products)
- Q72 – 81: Product Infusion

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** webpage.

Date	Manual Section	Add/ Remove/ Modify	Description
7/26/ 2024	2003:	Add	Version 2 of the 2003: Gene Therapy Product section of the Forms Instructions Manual released. Version 2 corresponds to revision 2 of the Form 2003.

Q1 – 6: 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.

Question 2: Is the product out of specification? (only for commercially available products)

This question is answered for commercially available. According to the product label, indicate if the product met specification release criteria, they are also defined as nonconforming products. The FDA specifies a set of criteria that the manufacturers need to comply with in order to define a product as within the specifications. For example, the product viability might be below the specified FDA criterium, however the product may be acceptable to be administered. In these situations, the manufacturer will contact the treating physician and inquire whether the product should still be shipped to the institution. Recipients are required to consent to infusion of a product out of specification. These infusions are done as part of an Expanded Access Protocol (EAP)-like format and in some rare instances as single patient Investigational New Product (IND).

This can be found in the patient records, or they will be enrolled into an out of specification protocol with a clinicaltrials.gov number (NCT ID). This NCT ID should be reported on the Pre-TED (2400) form.

Questions 3 – 6: 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.

  If the product infused in the commercially available product Zynteglo® or Skysona®, report the study subject ID (50x-xxx-xxxx) in the Gene therapy product ID field.

- **Batch number**: Batch numbers can be numeric or alphanumeric and are available with the information that comes with the product.

  If the product infused in the commercially available product Zynteglo® or Skysona®, report the total number of bags in the lot in the Batch number field.

- **Lot number:** Lot numbers can be numeric or alphanumeric and are available with the information that comes with the product.

  If the product infused in the commercially available product Zynteglo® or Skysona®, report the Drug Product (DP) lot number in the Lot number field.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Q7 – 15: 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 7 – 8 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 millimeter (mm3).

Questions 9 – 10 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 millimeter (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 11: Date of first collection for this mobilization

Report the first date (YYYY-MM-DD) 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.

Question 12-13: What agents were used to mobilize the recipient for this HCT? (check all that apply)

Specify the agents used in the mobilization event(s).

- **G-CSF:** granulocyte colony-stimulating factor, TBO-filgrastim, filgrastim, Granix®, Neupogen®
- **GM-CSF:** sargramostim, Leukine®
- **Pegylated G-CSF:** pegfilgrastim, Neulasta®
- **Motixafortide:** Aphexda®
- **Perlixafor:** Mozobil®
- **Combined with chemotherapy:** Systemic therapies used to enhance the stem cell product may include cyclophosphamide or ICE chemotherapy (Ifosfamide, carboplatin, and etoposide) with or without rituximab.
- **Anti-CD20:** rituximab, Rituxan®
- **Other agent**: If an agent was used but not listed above, select Other agent and specify.

Questions 14 – 15: 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 Gene Therapy Product (2003) form.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Q16 – 32: Product Processing / Manipulation

Product Processing and 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 Product Analysis.

Questions 16-19: 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. Refer to the question *Specify pharmaceutical / biotech company* on the form 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.
- **Other site**: If the gene product therapy was manufactured / process at a site not listed above, select this option, and specify.

Question 20: 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 21: Was the manipulated product cryopreserved?

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

Question 22: 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 23: Specify the type(s) of genetic manipulation

Specify the type(s) of genetic 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, specify the type of vector and transgene.
- **Gene editing**: Gene editing refers to the manipulation of genetic material by deleting, replacing, or inserting a DNA sequence. If this option is selected, continue with *Methodology*.
- **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 specify the other genetic manipulation.

Questions 24 – 25: 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. 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 26 – 27: 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. If the type of transgene is not known, select **Unknown**.

Questions 28 – 29 : 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 the other methodology.
- **Unknown**: If the methodology of gene editing is not known, select this this option

Questions 30 – 31: Specify the gene target

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

Question 32: 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)
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Q33 – 71: Product Analysis (All Products)

Reporting Multiple Instances of Product Analysis
To report multiple instances of product analysis, complete questions 33-71 by adding additional instances in FormsNet3[SM]

Question 33: 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 34: Date of product analysis

Report the date (YYYY-MM-DD) when the product was analyzed for each timepoint reported. The date of product analysis is not necessarily the date of the product infusion.

Question 35: 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), one decimal place is allowed.

Questions 36 – 37: 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 *Other cell type*.

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**.

Questions 38 – 39: 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 *Other cell type*.

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 above, select **Done** for the *Viability of CD34+ cells*, and report a viability of **100%**.

Questions 40 – 41: 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.

Questions 42 – 43: 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 in FormsNet3SM.

If no "other" cell types were quantified at the reported timepoint, select **Not done** and continue with Product Infusion

Questions 42 – 67: 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 of the "other" cell(s) was quantified. If **Done**, report the viability percent of cells and specify the method of testing for viability. 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.

Vector copy number (VCN)

The VCN for the infused product is only enabled if **Ex vivo transduction** is reported as a

genetic manipulation.

Questions 68 – 69: 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.

Percentage of gene edited cells

The percentage of gene edited cells for the infused product is only enabled if **Gene editing**.

Questions 70 – 71: Percentage of gene edited cells in the infused product

When a 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.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Q72 – 81: Product Infusion

Question 72: Date of manipulated product infusion

Report the date (YYYY-MM-DD) this product was infused. If the product was infused over multiple days, report the first date of infusion.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Questions 73 – 75: Was the entire volume of product infused?

The intent of this question is to capture if the product being infused was given in its entirety. If the entire volume of the product was not infused, select **No** and specify what happened to the reserved portion. If **Other fate** is selected, specify what happened to the reserved portion of the product.

Questions 76 – 77: 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 the other route. This option should be used sparingly since the only known method of infusion for gene therapy products is intravenous.

Question 78: 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 79: Date of unmanipulated product infusion

Report the date (YYYY-MM-DD) the unmanipulated product was infused. If the product was infused over multiple days, report the first date of infusion.

Questions 80 – 81: 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 the other route. This option should be used sparingly since the only known method of infusion for gene therapy products is intravenous.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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