4101: Post-Cellular Therapy Follow-Up

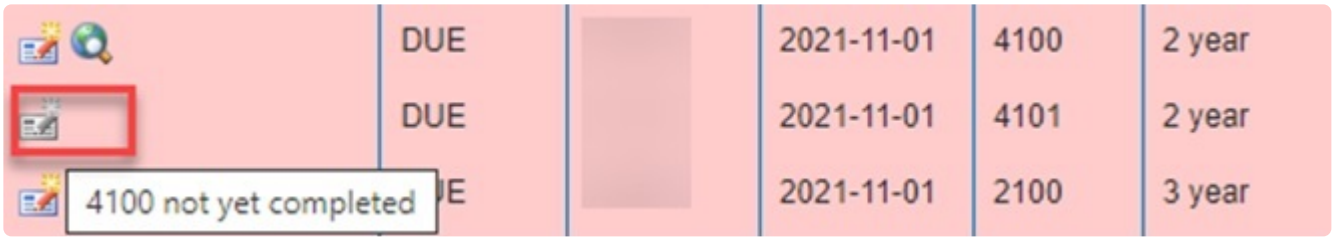
This form must be completed for all recipients of cellular therapy (non-HCT), including post-HCT DCI infusions selected for CRF level reporting. It will be completed in conjunction with the Cellular Therapy Essential Data Follow-Up (4100) form. For more information on TED and CRF level reporting, click here.

For recipients of hematopoietic cellular transplants, complete the appropriate HCT follow-up form. For recipients of Donor Lymphocyte Infusions (DLI), complete the Donor Lymphocyte Infusion (2199) form

The Post-Cellular Therapy Follow up Form focuses on research level data for each reporting period, including post-infusion hospital admission, antigen escape, current hematologic findings, and persistence of the cellular product.

> **Completing the Baseline Form**
> If the associated Post-CTED (4100) form has not yet been completed for the same time point, the edit form icon will appear disabled (see Figure 1 below). When the user hovers over the icon, it will display that the 4100 is not yet completed. The user must complete the Post-CTED (4100) form in order to enable the edit icon and allow for completion of the form. Data reported on Post-CTED (4100) form are used to validate questions on Cellular Therapy Essential Data Follow-Up (4100) form.

Figure 1. Disabled Edit Form Icon



Combined follow up
In scenarios where both HCT and cellular therapy forms are being completed, there are two scenarios where the Post-CTED (4100) and Post-Cellular Therapy Follow-Up(4101) forms are completed:

Example 1. Cellular therapy after HCT: completion of this form should be based on the time period in relation to the CT infusion date (i.e., 100 days after the CT infusion date). The visit ID and date of contact should match between the corresponding Post-HSCT Data (2100) or Post-Transplant Essential Data (2450).

Example 2. HCT after cellular therapy: completion of this form should be based on the time period in relation to the HCT infusion date (i.e., 100 days after the HCT infusion date). The visit ID and date of contact should match between the corresponding Post-HSCT Data (2100) or Post-Transplant Essential Data (2450).

Duplicate questions between HCT and cellular therapy forms may be disabled on the Post-CTED. A full list

of enabled/disabled fields can be found on the Combined Follow Up section of the Data Management Guide. Illustrations of the combined follow up scenarios can also be found the Guide.

Links to sections of form:
Q1: Product:
Q2-4: Survival:
Q5-22: Disease Relapse or Progression:
Q23-33: Current Hematologic Findings:
Q35-59: Persistence of Cells:

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 click here or reference the retired manual section on the Retired Forms Manuals webpage.

Date	Manual Section	Add/ Remove/ Modify	Description
1/24/ 2025	4101: Post-Cellular Therapy Follow-Up	Add	New blue note box above question 21: There are currently no commercially available persistence tests for the commercially available BCMA CAR-T products (e.g. Abecma, Carvykti. You may select **No** for the question *Were tests performed to detect persistence of the cellular product since the date of last report?*.
1/24/ 2025	4101: Post-Cellular Therapy Follow-Up	Modify	Modified blue note box above question 21: There is a ~~are currently no~~ commercially available persistence tests for the commercially available CD19+ CAR-T products (e.g. Kymriah, Yescarta, Tecartus, Breyanzi ~~, Abecma, Carvykti~~). You may still select **No** for the question *Were tests performed to detect persistence of the cellular product since the date of last report?* but please confirm if your site is using the new persistence test.
1/23/ 2024	4101: Post-Cellular Therapy Follow-Up	Add	Added the text in red: CAR-T cells that target antigens (e.g., CD19) on B-cells do not distinguish between cancerous and normal B-cells. As result, the recipient can develop B-cell aplasia (low number or absence of B-cells). B-cell aplasia can be used as a surrogate to track persistence of the product. If the recipient has B-cell aplasia, then the product may still be present. Examples include (but not limited to) “cellular immunology report”, “lymphocyte subsets”, or “B-cell panel” of applicable tests that will show B-cell populations.
1/15/ 24	4101: Post-Cellular	Modify	Added the text in red: Many cellular therapies are designed to target a specific tumor antigen(s). One mechanism of resistance to these cellular therapies includes antigen escape. This occurs when disease relapses and the tumor develops partial

	Therapy Follow-Up		or complete loss of the tumor antigen. This may be determined by testing (e.g. T-cell subset profile) on the blood and/or bone marrow showing absence of the tumor antigen targeted by the cellular therapy they received. Common testing methods are listed in question 6. Example 1: A recipient has a CD19 expressing disease prior to the cell therapy infusion, such as acute lymphoblastic leukemia (ALL) or non-Hodgkin lymphoma (NHL). The recipient is given a CD19-directed CAR T-cell therapy, achieves a CR then relapses. At the time of relapse, the T-cell subset profile shows the absence of CD19 B Cells. This means the leukemia/lymphoma cells no longer express CD19.
12/12/23	4101: Post-Cellular Therapy Follow-Up	Modify	Reformatted and created an example: **Example 1**: A recipient has a CD19 expressing disease prior to the cell therapy infusion, such as acute lymphoblastic leukemia (ALL) or non-Hodgkin lymphoma (NHL). The recipient is given a CD19-directed CAR T-cell therapy, achieves a CR then relapses. At the time of relapse their leukemia/lymphoma cells no longer express CD19.
8/22/23	4101: Post-Cellular Therapy Follow-Up	Modify	Update: Many cellular therapies are designed to target a specific tumor antigen(s). One mechanism of resistance to these cellular therapies includes antigen escape. This ~~is~~ occurs when disease relapses and the tumor develops partial or complete loss of the tumor antigen. An example is a recipient with acute lymphoblastic leukemia (ALL) that expresses the CD19 antigen prior to cellular therapy infusion.
8/22/23	4101: Post-Cellular Therapy Follow-Up	Add	New blue note box added under question 5: Antigen escape occurs in the context of relapse.
7/28/2023	4101: Post-Cellular Therapy Follow-Up	Add	Version 1 of the 4101: Post- Cellular Therapy Follow-Up section of the Forms Instruction Manual released. Version 1 corresponds to revision 1 of the form 4101.

Last modified: Feb 03, 2025

Q1: Product

Question 1: Name of Product: (for most recent cell therapy infusion)

The name of the product reported will be auto populated with the value reported on the Pre-Cellular Therapy Essential Data (4000) form. If the cellular therapy product infused is a commercially available or pre-commercial product, this question is used to enable questions related to toxicities and disable questions that do not apply.

Combined follow up
In scenarios where both HCT and cellular therapy forms are being completed, and the recipient has received the HCT after the cellular therapy, the product name should be for the prior cellular therapy product.

Section Updates:

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

Last modified: Jul 29, 2023

Q2-4: Survival

> ! The following questions will only be enabled if the cell therapy was reported on the Pre-Cellular Therapy Baseline Data (4001) form as planned as outpatient and can only be completed on the 100-day follow-up form. These questions will be skipped for all subsequent reporting periods.

Question 2: Was the recipient admitted to the hospital post-infusion?

The practice of outpatient cellular therapy infusions is increasing however there might still be the need for admission for cellular therapy toxicities. In order to capture if patients require admission following cellular therapy a date of admission and discharge will be collected.

Question 3: Date of first hospital admission:

Report the first date (YYYY-MM-DD) the recipient was admitted to the hospital post-infusion.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Question 4: Date of first discharge:

Report the date (YYYY-MM-DD) of first discharge after the first hospital admission.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Section Updates:

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

Last modified: Jul 29, 2023

Q5-9: Disease Relapse or Progression

Antigen escape
These question will enable only if the commercially available product Kymriah®, Yecarta®, Tecartus™, or Breyanzi™ is selected in question 1.
There is no current testing method for the BCMA CAR-T products (Abecma®, Carvykti™).

Question 5: Was there evidence of antigen escape?

Antigen escape occurs in the context of relapse.

Many cellular therapies are designed to target a specific tumor antigen(s). One mechanism of resistance to these cellular therapies includes antigen escape. This occurs when disease relapses and the tumor develops partial or complete loss of the tumor antigen. This may be determined by testing (e.g. T-cell subset profile) on the blood and/or bone marrow showing absence of the tumor antigen targeted by the cellular therapy they received. Common testing methods are listed in question 6.

Example 1: A recipient has a CD19 expressing disease prior to the cell therapy infusion, such as acute lymphoblastic leukemia (ALL) or non-Hodgkin lymphoma (NHL). The recipient is given a CD19-directed CAR T-cell therapy, achieves a CR then relapses. At the time of relapse, the T-cell subset profile shows the absence of CD19 B Cells. This means the leukemia/lymphoma cells no longer express CD19.

Report **Yes** if there was evidence of antigen escape.

If testing showed no evidence of antigen escape in the current reporting period, report **No**. If no testing was performed in the current reporting period, report **Not tested**.

Question 6-7: Method of detection of antigen escape (check all that apply)

Methods of detecting antigen escape include **Flow cytometry**, **Immunohistochemistry (IHC)** or **Other method**. Select the method(s) used to detect antigen escape. If **Other method** is selected, specify the method.

Question 8: Was documentation submitted to CIBMTR?

Indicate whether documentation of the antigen escape was submitted to CIBMTR (e.g., flow cytometry, immunohistochemistry report).

For further instructions on how to attach documents in FormsNet3℠, refer to the Formsnet3 Training Guide.

Question 9: Date of antigen escape

Report the date (YYYY – MM- DD) when testing first showed evidence of antigen escape. If the exact date is not known, use the process described in the General Instructions, General Guidelines for Completing Forms.

Section Updates:

Question Number	Date of Change	Add/ Remove/ Modify	Description	Reasoning (If applicable)
5	1/15/24	Modify	Added the text in red: Many cellular therapies are designed to target a specific tumor antigen(s). One mechanism of resistance to these cellular therapies includes antigen escape. This occurs when disease relapses and the tumor develops partial or complete loss of the tumor antigen. This may be determined by testing (e.g. T-cell subset profile) on the blood and/or bone marrow showing absence of the tumor antigen targeted by the cellular therapy they received. Common testing methods are listed in question 6. Example 1: A recipient has a CD19 expressing disease prior to the cell therapy infusion, such as acute lymphoblastic leukemia (ALL) or non-Hodgkin lymphoma (NHL). The recipient is given a CD19-directed CAR T-cell therapy, achieves a CR then relapses. At the time of relapse, the T-cell subset profile shows the absence of CD19 B Cells. This means the leukemia/lymphoma cells no longer express CD19.	Clarifying what type of test will show antigen escape
5	12/12/ 23	Modify	Updated red warning box above question five: These question will enable only if the commercially available product Kymriah®, Yecarta®, Tecartus™, or Breyanzi™ is selected in question 1. There is no current testing method for the BCMA CAR-T products (Abecma®, Carvykti™).	Clarifying context of question for BCMA products.
5	12/12/ 23	Modify	Reformatted and created an example: **Example 1**: A recipient has a CD19 expressing disease prior to the cell therapy infusion, such as acute lymphoblastic leukemia (ALL) or non-Hodgkin lymphoma (NHL). The recipient is given a CD19-directed CAR T-cell therapy, achieves a CR then relapses. At the time of relapse their leukemia/lymphoma cells no longer express CD19.	Clarifying the manual text and example.
5	8/22/23	Modify	Update: Many cellular therapies are designed to target a specific tumor antigen(s). One mechanism of resistance to these cellular therapies includes antigen escape. This ~~is~~ occurs when disease relapses and the tumor develops partial or complete loss of the tumor antigen. An example is a recipient with acute	Clarifying that antigen escape occurs in

			lymphoblastic leukemia (ALL) that expresses the CD19 antigen prior to cellular therapy infusion.	the context of relapse
5	8/22/23	Add	New blue note box added under question 5: Antigen escape occurs in the context of relapse.	Clarifying that antigen escape occurs in the context of relapse

Last modified: Jan 15, 2024

Q10-20: Current Hematologic Findings

! The following questions can only be completed on the 100 day, 6 month follow- up, 1 year, and 2 year forms. These questions will be disabled for all subsequent reporting periods.

* The following questions will only be answered if the recipient received lymphodepleting therapy as reported on the Pre-CTED (4000) form.

Question 10: Date of most recent complete blood count (CBC) sample drawn:

These questions are intended to determine the clinical status of the recipient at time of follow-up for this reporting period post cellular therapy. Testing may be performed multiple times post-infusion; report the most recent CBC obtained.

Questions 11-19: Complete blood count results available: (check all that apply)

For each cell type listed, checking the box will indicate a result is available. Provide the most recent laboratory values from the CBC on the date reported in the prior question.

WBC: The white blood cell count is a value that represents all the white blood cells in the blood. If the count is too high or too low, the ability to fight infection may be impaired.

Neutrophils: Neutrophils are a subtype of white blood cell that fights infection. The value on the laboratory report may be a percentage or an absolute value. If an absolute value is reported, divide it by the white blood cell count for a percentage. Neutrophils are also known as polymorphonuclear leukocytes (PMNs).

Lymphocytes: Lymphocytes are another subtype of white blood cell that fights infection. The value on the laboratory report may be a percentage of an absolute value. If an absolute value is reported, divide it by the white blood cell count for a percentage.

Hemoglobin: Hemoglobin is a molecule in red blood cells that delivers oxygen to tissues throughout the body. A low hemoglobin count is considered “anemia” and blood transfusions, or growth factors may be required to increase the hemoglobin level.

Hematocrit: The hematocrit is the percentage (sometimes displayed as a proportion) of red blood cells relative to the total blood volume. A low hematocrit may require red blood cell transfusions or growth factors. Indicate if the recipient received a red blood cell transfusion within 30 days prior to sample draw date.

If a hematocrit value is reported, also indicate if the recipient received a red blood cell transfusion within 30 days prior to the date of the CBC reported in question 17.

Platelets: Platelets are formed elements within the blood that help with coagulation. A low platelet count, called thrombocytopenia, may lead to easy bleeding or bruising. Thrombocytopenia may require platelet transfusions. Indicate if the recipient received a platelet transfusion within 7 days prior to testing.

If a platelet value is reported, also indicate if the recipient received a platelet transfusion within 7 days prior to the date of the CBC reported in question 19.

Questions 20: Did the recipient receive any growth factors <7 days before the date the sample was drawn?

Indicate if the recipient received any growth factor (e.g., GCS-F) within 7 days prior to the date the CBC sample was drawn. In the event of a long acting growth factor (e.g., pegfilgrastim (Neulasta®)), please answer this question as yes if the recipient received it within 14 days prior to the date the CBC sample was drawn.

Section Updates:

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

Last modified: Jul 29, 2023

Q21-45: Persistence of Cells

! This section pertains to the evaluation of persistence of a cellular product in the recipient and only applies to genetically modified cellular therapy products.

* There is a commercially available persistence tests for the commercially available CD19+ CAR-T products (e.g. Kymriah, Yescarta, Tecartus, Breyanzi). You may still select **No** for the question *Were tests performed to detect persistence of the cellular product since the date of last report?* but please confirm if your site is using the new persistence test.

* There are currently no commercially available persistence tests for the commercially available BCMA CAR-T products (e.g. Abecma, Carvykti). You may select **No** for the question *Were tests performed to detect persistence of the cellular product since the date of last report?*

Question 21: Were tests performed to detect persistence of the cellular product since the date of last report?

Methods such as PCR assays, flow cytometry (immunophenotyping) or immunohistochemistry can be used to detect direct persistence of the cellular product in the recipient.

It is possible to use other testing methods, such as monitoring B cells, as a surrogate for ongoing cellular therapy persistence. Surrogate testing should not be reported here. Monitoring of B cells can be reported in question 43.

Indicate **Yes** or **No** whether tests were performed to detect direct persistence of the cellular product in the current reporting period.

Question 22: Was persistence evaluated by molecular assay (PCR)?

Molecular assessment involves testing blood, bone marrow, tumor or other source for the presence of known molecular markers. Molecular assessments are the most sensitive test and involve amplifying regions of cellular DNA by polymerase chain reaction (PCR), typically using RNA to generate complementary DNA through reverse transcription (RT-PCR). The amplified DNA fragments are compared to a control, providing a method of quantifying log increase of genetic mutation transcripts. Each log increase is a 10-fold increase of gene transcript compared to control.

Indicate **Yes** or **No** whether molecular assay testing was performed to detect the persistence of the genetically modified cellular therapy product within the reporting period.

Question 23: Date Sample collected:

Report the date (YYYY-MM-DD) the sample was collected for molecular assay. If multiple tests were performed in the reporting period and

- all tests were negative, report the date of the first negative test result
- there were positive and negative results, report the date of the last positive test (do not report negative results)

If the exact date is unknown, please view General Instructions, “General Guidelines for Completing Forms”:#general-guidelines-for-completing-forms for
more information on reporting partial and unknown dates.

Questions 24-25: Specify the cell source: (check all that apply)

Specify the cell source of the sample collected for evaluation by molecular assay. Select all that apply. If multiple cell sources were used and persistence was detected in some but not all the samples, report ONLY the cell sources that were positive. If **Other source** is selected, specify the source.

Question 26: Were the infused cells detected?

Indicate **Yes** or **No** if the infused cells were detected by molecular assay.

Question 27: Was persistence evaluated by flow cytometry testing (immunophenotyping)?

Flow cytometry is a technique that can be performed on blood, bone marrow, or tissue preparations where cell surface markers can be quantified on cellular material. The nature of flow cytometry is to detect cells based on a specific probe. To report flow cytometry results, the test must have been performed to specifically detect the genetically modified cellular therapy product.

Indicate **Yes** or **No** if flow cytometry testing was performed to detect the persistence of the genetically modified cellular therapy product within the reporting period.

Question 28: Date sample collected:

Report the date (YYYY-MM-DD) the sample was collected for flow cytometry testing (immunophenotyping). If multiple tests were performed in the reporting period and

- all tests were negative, report the date of the first negative test result
- there were positive and negative results, report the date of the last positive test (do not report negative results)

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

Question 29-30: Specify the cell source (check all that apply)

Specify the cell source of the sample collected for evaluation by flow cytometry. Select all that apply. If multiple cell sources were used and persistence was detected in some but not all the samples, report ONLY the cell sources that were positive. If Other source is selected, specify the source.

Question 31: Were the infused cells detected?

Indicate **Yes** or **No** if the infused cells were detected by flow cytometry.

Question 32: Was persistence evaluated by immunohistochemistry?

Immunohistochemistry is a process that uses antibodies to test for certain antigens (markers) in a sample. When the antibodies bind to the antigen in the tissue sample, the enzyme or dye is activated, and the antigen can then be seen under a microscope.

Indicate **Yes** or **No** if immunohistochemistry testing was performed to detect the persistence of the genetically modified cellular product within the reporting period.

Question 33: Date sample collected:

Report the date (YYYY-MM-DD) the sample was collected for immunohistochemistry. If multiple tests were performed in the reporting period and

- all tests were negative, report the date of the first negative test result
- there were positive and negative results, report the date of the last positive test (do not report negative results)

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

Question 34-36: Specify the cell source:

Specify the cell source of the sample collected for evaluation by immunohistochemistry. Select all that apply. If multiple cell sources were used and persistence was detected in some but not all the samples, report ONLY the cell sources that were positive. If **Other source** is selected, specify the source.

Question 36: Were the infused cells detected?

Indicate **Yes** or **No** if the infused cells were detected by immunohistochemistry testing.

Questions 37-38: Was persistence evaluated by other method?

Indicate **Yes** or **No** if persistence of cells was tested by a method not listed above. If **Yes**, specify the other method used to evaluate persistence of cells.

Question 39: Date sample collected:

Report the date (YYYY-MM-DD) the sample was collected for the other method. If multiple tests were performed in the reporting period and

- all tests were negative, report the *date of the first negative test result*
- there were positive and negative results, report the *date of the last positive test (do not report negative results)*

If the exact date is unknown, please view General Instructions, “General Guidelines for Completing Forms”:#general-guidelines-for-completing-forms for more information on reporting partial and unknown dates.

Question 40-41: Specify the cell source:

Specify the cell source of the sample collected for evaluation by other method. Select all that apply. If multiple cell sources were used and persistence was detected in some but not all the samples, report ONLY the cell sources that were positive. If **Other source** is selected, specify the source.

Question 42: Were the infused cells detected?

Indicate **Yes** or **No** if the infused cells were detected by the other method being reported in these questions.

> ✻ The following questions will only enable for the commercial CAR-T products that target CD19+ cells (Kymriah® or Yescarta®, Tecartus™, Breyanzi™)

Question 43: Were B-cell counts monitored after infusion?

CAR-T cells that target antigens (e.g., CD19) on B-cells do not distinguish between cancerous and normal B-cells. As result, the recipient can develop B-cell aplasia (low number or absence of B-cells). B-cell aplasia can be used as a surrogate to track persistence of the product. If the recipient has B-cell aplasia, then the product may still be present. Examples include (but not limited to) “cellular immunology report”, “lymphocyte subsets”, or “B-cell panel” of applicable tests that will show B-cell populations.

Indicate **Yes** or **No** if B-cell counts were monitored during the current reporting period.

Question 44: Was there B-cell recovery?

A guideline for B-cell aplasia is a B-cell count of < 50 cells/μL of blood., If B-cell aplasia was identified and B-cells subsequently recovered (>50 cells/uL), select **Yes**. If B-cells never recovered, report **No**, or select **Unknown** if B-cell recovery is not documented.

B-cell counts in the blood do vary with age, and children have much higher counts than adults. The younger the child, the higher the concentration.

Question 45: Date of B-cell recovery

Report the date (YYYY-MM-DD) the flow cytometry report showed B-cell recovery.

Section Updates:

Question Number	Date of Change	Add/ Remove/ Modify	Description	Reasoning (If applicable)
21	1/24/ 2025	Add	New blue note box above question 21: There are currently no commercially available persistence tests for the commercially available BCMA CAR-T products (e.g. Abecma, Carvykti. You may select **No** for the question *Were tests performed to detect persistence of the cellular product since the date of last report?*.	Update for new commercially available CD19+ CAR-T persistence test, there are still no tests for BCMA products.
21	1/24/ 2025	Modify	Modified blue note box above question 21: There is a ~~are currently no~~ commercially available persistence tests for the commercially available CD19+ CAR-T products (e.g. Kymriah, Yescarta, Tecartus, Breyanzi ~~, Abecma, Carvykti~~). You may still select **No** for the question *Were tests performed to detect persistence of the cellular product since the date of last report?* but please confirm if your site is using the new persistence test.	Update for new commercially available CD19+ CAR-T persistence test.
43	1/23/ 2024	Add	Added the text in red: CAR-T cells that target antigens (e.g., CD19) on B-cells do not distinguish between cancerous and normal B-cells. As result, the recipient can develop B-cell aplasia (low number or absence of B-cells). B-cell aplasia can be used as a surrogate to track persistence of the product. If the recipient has B-cell aplasia, then the product may still be present. Examples include (but not limited to) “cellular immunology report”, “lymphocyte subsets”, or “B-cell panel” of applicable tests that will show B-cell populations.	Clarification of applicable report names.

Last modified: Feb 03, 2025