Instructions for Neuroblastoma Pre-Infusion (2026)

This section of the CIBMTR Forms Instruction Manual is intended to be a resource for completing the Neuroblastoma Pre-Infusion (2026) Form.

Neuroblastoma Pre-Infusion

The Neuroblastoma Pre-Infusion Data (2026) Form is one of the Comprehensive Report Forms. This form captures neuroblastoma specific pre-infusion data such as the recipient's clinical and laboratory findings at the time of diagnosis and prior to the start of the preparative regimen, pre-infusion treatments administered, and disease manifestations prior to the preparative regimen.

This form must be completed for all recipients randomized to the Comprehensive Report Form (CRF) track whose primary disease is reported on the Disease Classification (2402) Form as Neuroblastoma under .

MIBG Therapy and Additional Infusion of Cells
MIBG therapy has been used to deliver targeted radiation to patients with neuroblastoma. This therapy destroys tumors while sparing normal, healthy tissue. MIBG therapy is currently may be used to treat newly diagnosed, used to treat relapsed or refractory neuroblastoma and is being studied as treatment for newly diagnosed high risk patients.
Treatment for high-risk neuroblastoma includes the following:
Induction therapy: Chemotherapy, stem cell collection, surgical resection of primary tumor
Consolidation therapy: High-dose chemotherapy followed by Autologous HCT, radiation therapy
Maintenance therapy: Immunotherapy, Cis-Retinoic acid
Clinical trials have randomized newly diagnosed high risk neuroblastoma patients with MIBG-avid disease to either standard induction therapy or standard induction therapy with the addition of I-131 MIBG. Since the most common side effect of MIBG therapy is low blood counts, the patient's hematopoietic progenitor stem cells (HPCs or CD34+ cells) are collected and stored prior to the first treatment with MIBG. These HPCs are then available for HCT or as a "rescue" following MIBG therapy.
Effective November 2020, if a neuroblastoma recipient undergoing induction therapy with MIBG therapy receives an infusion of HPCs / CD34+ cells as a "rescue" due to low blood counts, centers no longer need to report this as an HCT.

Links to Sections of Form

Manual Updates:

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

To review the historical Manual Change History for this manual, reference the retired manual section on the Retired Forms Manuals webpage.

Date	Manual Section	Add/Remove/Modify	Description
12/12/2025	Neuroblastoma Pre-Infusion	Modify	Version 2 of the 2026: Neuroblastoma Pre-Infusion section of the Forms Instructions Manual released. Version 2 corresponds to revision 3 of the Form 2026.

Q1: Subsequent Infusion

Question 1: Is this a report of a second or subsequent infusion for the same disease?

Indicate if the reporting of this infusion is of a subsequent infusion for the same disease subtype.

Report **No** in any of the following scenarios:

- This is the first infusion reported to the CIBMTR;
- This is the first infusion given to treat the recipient's current disease; or
- This is a second or subsequent infusion for the same disease and this baseline disease insert was not completed for the previous transplant (e.g., recipient was on TED track for the prior infusion, prior infusion was autologous with no consent, etc.).

If this is a report of a subsequent infusion for the same disease and this baseline lymphoma disease insert was completed previously, report **Yes**.

Section Updates

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

Q2 – 61: Clinical and Laboratory Characteristics at Diagnosis

Questions 2 – 31: Specify the site(s) of primary tumor(s) at diagnosis

For each site, specify if the primary tumor was identified at this location at diagnosis. If the primary tumor was identified at the site, select **Yes** and report the number of tumors present.

If the primary tumor was located at site is not listed, indicate **Yes** for *Other site*, report the number of tumors present at diagnosis and specify the location.

If the location of primary tumor(s) at diagnosis is unknown, select **No** for each site, and report **Yes** for *Location of primary tumor(s) unknown.*

Question 32: Were metastases present at diagnosis?

Metastases can develop when cancer cells break away from the main tumor and enter the bloodstream or lymphatic system. Indicate if metastases were present at diagnosis.

This **Unknown** option should be used sparingly and only when no diagnostic information is available.

Questions 33 – 47: Specify the site(s) of metastases

For each site, specify if the site of metastatic neuroblastoma present at diagnosis.

If metastatic disease was present at a site not listed, report **Yes** for *Other site* and specify the site.

Questions 48 – 52: Specify radiographic tests used to evaluate the disease status at diagnosis

Radiologic assessments are imaging techniques used to assess disease at diagnosis, typically for lymphomas or solid tumors. A multimodal imaging approach is often taken

when evaluating neuroblastoma. CT, MRI, scintigraphy, and skeletal surveys are commonly used.

For each radiologic assessment, indicate if any of the listed radiologic tests were performed to evaluate the disease status at diagnosis.

See below for definitions and examples of each method of assessment:

- CT scan: Uses computer processing to turn numerous x-rays taken from many different angles into cross-sectional images; these scans can be useful for identifying abnormal structural features or pathologically enlarged organs or tissues.
- Magnetic resonance imagining (MRI): Magnetic resonance imaging (MRI) is an imaging technique used to form pictures of the anatomy and the physiological processes of the body.
- I-meta-iodobenzylguanidine scan (MIBG): Uses radioactive tracers for imaging +/- tissue destruction. These scans are specific to andrenergic tissues, which are those nervous system tissues involved in epinephrine and norepinephrine production and reception.
- Skeletal survey: Or “bone survey”, is comprised of a series of x-rays taken to examine all the bones in the body.
- Technetium scan: Technetium (Tc-99m) is an isotope commonly used as a tracer in imaging scans to detect how certain parts of the body are functioning. Tc-99m scans are often used to detect a wide range of conditions such as tumors, heart disease, thyroid abnormalities and kidney conditions.

Question 53: Were any biopsies performed at diagnosis?

Indicate if any biopsies were performed at diagnosis or prior to the first treatment for neuroblastoma. If biopsies were not performed at diagnosis or prior to the first treatment or it is not known if one was performed, select **No**.

Questions 54 – 58: Specify the biopsy site(s) positive for neuroblastoma

For site, specify whether each biopsy was positive for neuroblastoma. If a biopsy site was tested and negative for neuroblastoma, the site was not biopsied, or unknown if biopsied, indicate **No**.

If a biopsy was positive for neuroblastoma at a site not listed, indicate **Yes** for *Other site* and specify.

Question 59: Specify the histologic findings by Shimada classification

The Shimada classification divides tumors into **Stroma-rich** and **Stroma-poor** categories according to their organizational pattern. Stroma refers to Schwann cells associated with neuroblastoma cells.

Specify the Shimada classification for the positive biopsy(ies) specified above using the following below:

- **Stroma-rich**: Percentage of tumor stroma ≥ 50%
- **Stroma-poor**: Percentage of tumor stroma < 50%

This information is likely to be found in a histopathology report from a tissue biopsy; however, if the Shimada classification is unclear, seek physician clarification.

If the histologic findings by the Shimada classification are not known, select **Not classified / unknown**.

Question 60: Specify histology

Specify the histology of the stroma-rich biopsy as either **Nodular** or **Well differentiated / intermixed**. This classification is based on the morphology of immature elements and might be included in a histopathology report. However, clinician clarification may be necessary.

Question 61: Specify histology

Specify if histology of the stroma-poor biopsy is considered **Favorable** or **Unfavorable**. This classification is typically based on the recipient's age at diagnosis, degree of maturation, and the mitosis-karyorrhexis index (count of cells undergoing mitosis or karyorrhexis) of the neuroblastic cells. This information might be included in a histopathology report; however, clinician input may be necessary if the histology is not documented within the biopsy report.

Section Updates

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

Q62 – 228: Laboratory Values at Diagnosis of Neuroblastoma

Laboratory Values at Diagnosis
The intent of these questions is to capture the laboratory findings at the time of diagnosis. If multiple studies were performed prior to the institution of therapy, report the values closest to the diagnosis date of neuroblastoma.

Questions 62 – 69: Laboratory values at diagnosis

For each value below, indicate if the result was known at diagnosis. If **Known**, specify the value and the units of measurement, taking care to convert them to a unit available on the form, if necessary.

- 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.
- Hemoglobin (untransfused): 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. Report a hemoglobin value from diagnosis without supported blood transfusions. If there is no hemoglobin value available without transfusions report **Not known**.
- Platelets (untransfused) : 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. Report a platelet count from diagnosis without supported transfusions. If there is no platelet count available without transfusions report **Not known**.
- Hematocrit: The hematocrit is the percentage (sometimes displayed as a proportion) of red blood cells relative to the total blood volume. Low hematocrit may require red blood cell transfusions or growth factors.

Questions 70 – 83: Specify the following tumor marker analyses performed at diagnosis

Tumor markers, also known as biomarkers, are substances produced by cancer tissue or by the body in response to cancer at higher-than-normal levels. In certain situations, these substances can be used to detect and monitor disease due to their elevated presence in blood, urine, and/or tissue. The labs listed below have been identified as potential tumor markers for neuroblastoma.

For each tumor marker, indicate if it was analyzed at diagnosis. If analyzed, select **Known**, specify the value, unit of measurement and upper limit for the lab, if applicable. If the analysis was performed and the value is not known or it is unknown if performed, select **Not known**.

- Homovanillic acid (HVA): Catecholamines (e.g. epinephrine/adrenaline) are secreted as hormones from the adrenal medulla. Neuroblastomas typically produce excessive levels of these catecholamines. After catecholamines are secreted they are broken down into metabolites including Homovanillic acid (HVA) and Vanillylmandelic acid (VMA). Both HVA and VMA are excreted in the urine. As a result, elevated levels of HVA and VMA detected by urinary analysis can be indicative of neuroblastoma.

- Neuron specific enolase (NSE): A glycolytic enzyme (enolase) specific to neuronal-type tissues. NSE may be excessively expressed by neuroblastomas and indicative of disease.
- Serum ferritin: Ferritin is a blood protein that contains iron. A ferritin level indicates how much iron a person's body is storing. If the ferritin level is lower than normal, it indicates the body's iron stores are low (iron deficiency). If the ferritin level is higher than normal it could indicate hemochromatosis, a condition that causes the body to store too much iron. Other causes of an elevated ferritin level include liver disease, acute and chronic inflammatory conditions, malignancy (neuroblastoma) to name a few.
- Vanillylmandelic acid (VMA): Both HVA and VMA are excreted in the urine. As a result, elevated levels of HVA and VMA detected by urinary analysis can be indicative of neuroblastoma.
- LDH: Lactate dehydrogenase is an enzyme found in the cytoplasm of almost all tissues, which converts L-lactate into pyruvate, or pyruvate into L-lactate depending on the oxygen level. For some diseases, high levels indicate active disease (e.g., lymphoma, multiple myeloma and neuroblastoma).
- Other tumor marker analysis: If testing for a tumor marker was performed at diagnosis and is not listed above, select **Known**, and specify the other tumor marker, value and units of measurements. Examples of other testing can include Chromogranin A (CgA) or Neuropeptide Y (NpY)

Question 84: Was a DNA analysis performed at diagnosis?

DNA analysis is useful in further characterizing neuroblastoma and can provide prognostic and therapeutic value. Types of DNA analysis include ploidy testing to measure total cell DNA, detecting the presence of proto-oncogenes, and quantifying amplification.

Indicate if DNA analysis was performed at diagnosis.

Questions 85 – 88: Specify the tissue(s) analyzed

For each tissue, specify if DNA analysis was performed on the bone marrow, the first-degree tumor (primary tumor) at diagnosis. If DNA analysis was performed at diagnosis on a tissue type other than bone marrow or first-degree tumor, select **Yes** for *Other tissue* and specify.

Questions 89 – 92: Specify ploidy

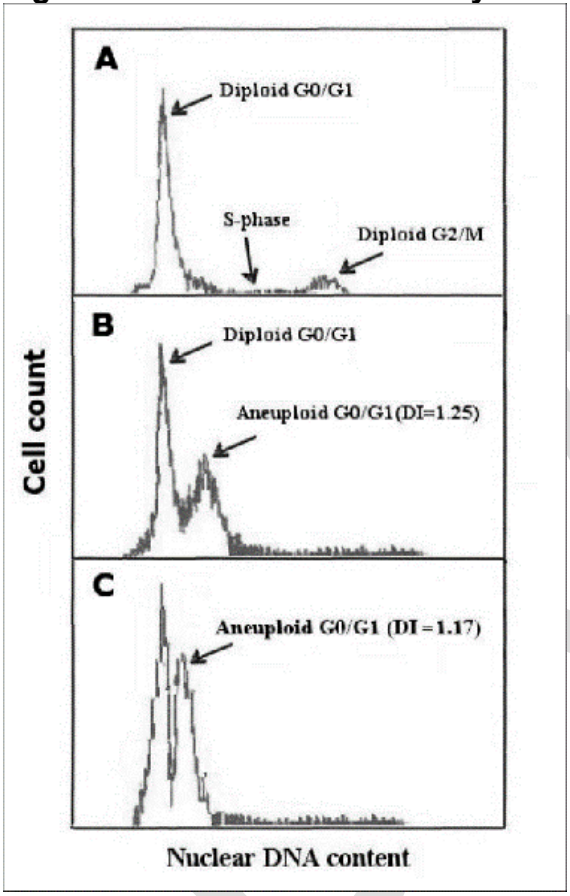
Ploidy refers to the number of chromosome sets in a cell. Examples of ploidy includes the modal number and the DNA index. Karyotyping is a technique often used to determine a cell's ploidy and proliferative activity while flow cytometry may measure the DNA index.

The modal number is the number of chromosomes present. A normal diploid cell has two sets of chromosomes or 46 total chromosomes. The “46” is the modal number.

The DNA index is a ratio between the DNA content of a normal cell (1) and a tumor cell (occasionally differing from 1) dictated via flow cytometry. See Figure 1 below for an example of a DNA index within a flow cytometry report.

Specify if the modal number and DNA index were known at diagnosis and specify the value.

Figure 1. DNA index in a flow cytometry report.



Questions 93 – 99: Specify any methods used to determine the presence of proto-oncogenes

Proto-oncogenes are normal genes that typically encode proteins with regulatory roles in cell growth and cell death. When proto-oncogenes are altered, they can contribute to cancer. N-myc and trk A are proto-oncogenes associated with neuroblastoma. This is often assessed by FISH. Specify any methods used to assess the presence of proto-oncogenes a diagnosis.

- N-myc amplification: An oncogene that encodes for the n-myc protein. This proto-oncogene amplification is often associated with poor prognosis / outcomes for neuroblastoma. If N-myc amplification was **Known**, indicate if proto-oncogenes were detected and specify the copy number. If N-myc amplification was not assessed or unknown at diagnosis, select **Not known**.
- trk A expression: A protein that is encoded is encoded by the NTRK1 gene. Expression of this protein in tumors is often associated with a favorable prognosis / outcome. If trk A expression was **Known**, specify the expression of proto-oncogenes as documented in the report. Use the following guidelines:
    - **High**: Expression detected in high levels
    - **Low**: Expression detected in low levels
    - **Absent**: Expression absent

  If trk A expression was not assessed or unknown at diagnosis, select **Not known**.
- Other molecular abnormalities: Specify if other molecular abnormalities were present at diagnosis. If **Yes**, specify the molecular abnormality(ies). If other molecular abnormalities were assessed and not detected, select **No**. If it is not known if testing for other molecular markers were performed at diagnosis or if testing was performed but the results are not known, select **Unknown**.

Question 100: Was a cytogenetic analysis performed at diagnosis?

Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of known chromosomal abnormalities that reflect the recipient's disease.

Testing methods you may see include conventional chromosome analysis (karyotyping). For more information about cytogenetic testing and terminology, see Appendix C: Cytogenetics.

Indicate whether a karyotype analysis was obtained at diagnosis using the guidelines provided below. Do not report any testing performed after the treatment for neuroblastoma has started.

- **Yes**: Karyotype was obtained at diagnosis and metaphases were evaluable.
- **Yes, but no evaluable metaphases**: Karyotype was performed at diagnosis, but metaphases were not evaluable.
- **No**: Karyotype was not performed at diagnosis.
- **Unknown**: It is unknown if karyotype was performed at diagnosis.

Questions 102 – 104: Specify the tissue(s) analyzed

For each tissue, indicate if it karyotyping was performed at the time of diagnosis.

If a tissue type was analyzed and not listed as an option, select **Yes** for *Other tissue* and specify.

If karyotyping was not performed or it is not known if performed on the tissue, select **No**.

Questions 105 – 106: Number of metaphases

Metaphase is a cell life cycle stage indicative of mitotic activity (cell division). A normal metaphase includes 46 chromosomes (46, XX or 46, XY).

Specify if the number of metaphases was known at the time of diagnosis. If **Known**, report the number of metaphases.

Question 107: Was the karyotype abnormal?

Indicate if the karyotype was abnormal at diagnosis. If abnormalities were not identified or it is unknown if abnormalities were present at diagnosis, report **No** or **Unknown**, respectively.

Questions 109 – 114: Specify the karyotype abnormalities

For each of the karyotype abnormalities, indicate if the abnormality was identified at diagnosis. If the abnormality was not detected at diagnosis, select **No**. If it is not known if the abnormality was identified at diagnosis, report **Unknown**. This option should be used sparingly and only when there is no information available about the results of the cytogenetics performed at diagnosis.

If an abnormality was identified but is not listed, report **Yes** for *Other abnormality* and specify the abnormality.

Staging at Diagnosis
Determining the staging may require examination of outside or older medical records. Similarly, interpretation of these data may require clinician input.

Question 114: Specify the International Neuroblastoma Staging System (INSS) disease stage at diagnosis

The International Neuroblastoma Staging System (INSS) is a standardized way to classify the extent of the cancer and considers surgical excision of the tumor. Specify the recipient's INSS stage at diagnosis. The stage may be documented in progress notes or can be confirmed with a clinician using Table 1 below.

If the INSS stage at diagnosis was not known or if only the Pediatric Oncology Group (POG) stage or the Evans Group stage is known, select **Unknown**.

Table 1. International Neuroblastoma Staging System

Stage	Definition

Stage 1	Localized tumor with complete gross excision, with or without microscopic residual disease; representative ipsilateral lymph nodes negative for tumor microscopically (nodes attached to and removed with the primary tumor may be positive)
Stage 2A	Localized tumor with incomplete gross excision; representative ipsilateral nonadherent lymph nodes negative for tumor microscopically.
Stage 2B	Localized tumor with or without complete gross excision, with ipsilateral nonadherent lymph nodes positive for tumor; enlarged contralateral lymph nodes must be negative microscopically.
Stage 3	Unresectable unilateral tumor infiltrating across the midline (defined as the vertebral column; tumors originating on one side and crossing the midline must infiltrate to or beyond the opposite side of the vertebral column), with or without regional lymph node involvement; or localized unilateral tumor with contralateral regional lymph node involvement; or midline tumor with bilateral extension by infiltration (unresectable) or by lymph node involvement.
Stage 4	Any primary tumor with dissemination to distant lymph nodes, bone, bone marrow, liver, skin and/or other organs (except as defined for stage 4S).
Stage 4S	Localized primary tumor (as defined for Stages 1, 2A, or 2B), with dissemination limited to skin, liver, and/or bone marrow (marrow involvement in Stage 4S should be minimal i.e., <10% of total nucleated cells identified as malignant on bone marrow biopsy or on marrow aspirate; more extensive marrow involvement would be considered to be Stage 4; the MIBG scan (if performed) should be negative in the marrow). Stage 4S is limited to infants < 1 year of age.

Pediatric Oncology Group and Evans Group Staging Systems

If the INSS cannot be determined, then the Pediatric Oncology Group (POG) Staging System or The Evans Group Staging System may be reported

Question 115: Specify the POG Stage

Using Table 2 below, specify if the recipient's POG stage at diagnosis is known, and report the stage.

Table 2. Pediatric Oncology Group

Stage	Definition
A	Complete gross excision of primary tumor, margins histologically negative or positive. Intracavitary lymph nodes not intimately adhered to and removed with resected tumor must be histologically free of tumor. If primary is in abdomen or pelvis, liver must be histologically free of tumor.

B	Incomplete gross resection of primary. Lymph nodes and liver must be histologically free of tumor.
C	Complete or incomplete gross resection of primary. Intracavitary nodes (cavity of primary) histologically positive for tumor. Liver histologically free of tumor.
D	Disseminated disease beyond intracavitary nodes in bone marrow, bone, liver, skin, or lymph nodes beyond cavity containing primary tumor.

Question 116: Specify the Evans Stage

Using Table 3 below, specify if the recipient's Evans stage at diagnosis is known, and report the stage.

Table 3. Evans Stage

Stage	Definition
I	Tumor confined to the organ structure of origin
II	Tumors extending in continuity beyond the organ or structure of origin but not crossing the midline. Regional lymph nodes on the ipsilateral side may be involved
III	Tumors extending in continuity beyond the organ or structure or origin but not crossing the midline. Regional lymph nodes on the homolateral side may be involved
IV	Remote disease involving skeleton, soft tissues, distant lymph node groups, etc.
IV-S	Patients with local stage I or II disease but who have remote disease confined to one or more the following: liver, skin, bone marrow, (with no evidence of bone metastases on complete skeletal survey).

Question 117: Are other family members known to have neuroblastoma or ganglioneuroma?

Gene mutations that increase the risk of developing neuroblastoma can be inherited. Indicate whether immediate family members or other relatives have been diagnosed with neuroblastoma or ganglioneuroma.

Questions 118 – 125: Specify the family member(s) diagnosed with neuroblastoma or ganglioneuroma

For each family members listed, indicate if they were diagnosed with neuroblastoma or ganglioneuroma.

If a sibling is diagnosed with neuroblastoma or ganglioneuroma, specify the number of sisters and / or brothers affected. If the number of siblings affected is not known, select **Number of affected sisters unknown** and / or **Number of affected brothers unknown**.

If a relative not listed was diagnosed with a neuroblastoma or ganglioneuroma, indicate **Yes** for *Other relative* and specify the relationship.

If it is not known if a family member is diagnosed with a neuroblastoma or ganglioneuroma, select **Unknown**. This option should be used sparingly and only when the health history is not known for the family member.

Question 126: Does the recipient have a family history of other genetic diseases in first-degree blood relatives?

Indicate if the recipient has a family history of other genetic diseases in first-degree blood relatives. First degree relatives include parents, siblings and offspring.

Questions 127 – 132: Specify the diagnoses present in the immediate family

Specify the immediate family member's genetic disease(s). If it is not known if any immediate family members were diagnosed with the genetic, select **Unknown**.

- Beckwith-Wiedemann (EMG) syndrome: A common overgrowth / cancer predisposing disorder caused by changes on chromosome 11. EMG syndrome is characterized by a wide arrange of physical symptoms including; increased growth and birth weight, enlargement of internal organs and abdominal wall defects.
- Nesidioblastosis: A rare disorder of the beta cells of the pancreas, causing persistent hyperinsulinemic hypoglycemia.
- Neurofibromatosis: A genetic disorder in which causes tumors to form within the nervous system (brain, spinal cord, nerves, etc.)
- Trisomy 18: A chromosomal disorder associated with physical abnormalities such as decreased growth and birth weight, heart defect and abnormally shaped head and small facial features.
- Other disease: If an immediate family member was diagnosed with a genetic disease not listed above, select **Yes** and specify the disease. Examples of other genetic diseases include PHOX2B mutation, neurocristopathy, and ALK germline mutation.

Question 133: Did spontaneous regression of the recipient's tumor occur?

In certain cases of neuroblastoma, generally those with early disease onset (<1 year of age), spontaneous regression of the disease is possible.

Indicate whether spontaneous regression of the recipient's tumor occurred prior to infusion.

Question 134: Did the recipient undergo surgery as part of the initial disease treatment plan?

Treatment for neuroblastoma is determined based on the recipient's risk group:

- Low-risk neuroblastoma is typically treated with surgery, chemotherapy, or a combination of the two. In certain instances, observation may be the course of action.
- Intermediate-risk neuroblastoma is typically treated with surgery, chemotherapy, a combination of surgery and chemotherapy, or less commonly, radiotherapy.
- High-risk neuroblastoma therapy can include a regimen of surgery, chemotherapy, radiotherapy, hematopoietic cell transplant, cis-retinoic acid and immunotherapy.

Indicate if surgery was performed as part of initial treatment (either at diagnosis or after induction therapy).

If it is not known if surgery was completed as part of the initial treatment plan, select **No**.

Question 135: Specify surgery timepoint

Indicate the timepoint when the surgery was performed.

Question 136: Specify the histological diagnosis of resected tissue

Neuroblastic tumors can be classified as anglioneuroblastomas, ganglioneuromas, or neuroblastomas. These neuroblastic tumors differ histologically in degree of cellular and extracellular maturation.

- **Ganglioneuroblastoma**: Consists of mature gangliocytes and immature neuroblasts resulting in intermediate aggressive behavior.
- **Ganglioneuroma**: The most benign tumor of the three and exhibits greater degrees of maturation.
- **Neuroblastoma**: The most malignant and immature of the three tumors.

Specify the histological diagnosis of the resected tissue.

Questions 137 – 152: Specify the site(s) of surgery

For each site, specify whether each of the anatomical locations listed was a site of surgery for disease. If surgery was performed at a listed site, indicate **Yes**, specify the extent using Table 4 below, and date of surgery. If surgery was performed at a site not listed, select **Yes** for *Other site*, specify the extent, date of surgery, and surgery site.

Table 4. Extent of Surgery

Gross	> 95% resection, no radiographic residual tumor
Near	90 – 95% resection, minimal radiographic residual tumor
Subtotal	51 – 89% resection, moderate radiographic residual tumor
Partial	10 – 50% resection, significant radiographic residual tumor
Biopsy	< 10 % resection, no radiographic change from pre-op

Question 153: Did the recipient undergo radiotherapy as part of the initial disease treatment plan?

Radiation therapy utilizes high-energy radiation to kill cancer cells. Indicate whether radiotherapy was used as part of the initial disease treatment plan. If radiotherapy was not used or if no information is available to determine if radiotherapy was given as part of the initial disease treatment plan, report **No** or **Unknown**.

Questions 154 – 160: Specify the site(s) of radiotherapy

For each site, indicate if radiation therapy was given. For each site radiotherapy was given to specify the total number of fractions given to this site and the dose per fraction in centigrays (cGy / rads).

If the site of radiotherapy is not listed, select **Yes** for *Other site* and specify.

Lines of Therapy Reporting Instruction Overview
Refer to the Lines of Therapy reporting instruction overview for information on lines of therapy reporting.

Question 161: Did the recipient undergo chemotherapy as part of the initial disease treatment plan?

Indicate if the recipient received chemotherapy as part of the initial disease treatment plan.

If chemotherapy was not given or if no information is available to determine if chemotherapy was given as part of the initial disease treatment plan, report **No** or **Unknown**.

Question 162: Specify the date the first chemotherapy cycle began

Chemotherapy is usually administered in cycles with rest periods between the cycles. This enables cancer cells to be attacked at vulnerable times and provides healthy cells adequate time to recover from the damage. A cycle can last one or more days and may

repeat weekly, bi-weekly, monthly, etc. A chemotherapy course may consist of multiple cycles.

Report the date the first chemotherapy cycle began.

If the start date is partially known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

If the therapy start date is not known and cannot be estimated, select the **Date the first chemotherapy cycle began unknown**.

Question 163: Specify the date the last chemotherapy cycle began

Report the date when the last chemotherapy cycle given as part of the initial treatment plan began.

If the start date of the last cycle is partially known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

If the therapy end date is not known and cannot be estimated, select **Date the last chemotherapy cycle began unknown**.

Question 164: Specify the total number of chemotherapy cycles given

A chemotherapy course may consist of multiple cycles. Report the total number of chemotherapy cycles as part of the initial treatment plan the recipient received.

If the therapy is not given in cycles or the number of cycles is not known, check the **Number of chemotherapy cycles given unknown**.

Questions 165 – 176: Specify the treatment(s) given

Treatments vary based on protocol. A treatment may consist of a single drug or a combination of drugs. Additionally, the drugs may be administered on one day, over consecutive days, or continuously.

For each drug listed, indicate if the recipient received the therapy as part of the initial treatment plan. If the recipient received an agent that is not listed, select **Yes** for *Other treatment* and specify the treatment. Report the generic name and not the brand name.

Question 177: Specify the best response to chemotherapy

Based on the International Neuroblastoma Response Criteria, specify the best response to the initial treatment plan. The best response is determined by a disease assessment,

such as radiology or pathology and may occur during the therapy or after, but prior to starting the next treatment / infusion.

If the disease status was not reassessed prior to starting the next treatment or infusion, select **Unknown**.

Questions 178 – 179: Did neuroblastoma recur?

Indicate if neuroblastoma recurred (after achieving a CR) after the initial disease treatment plan and prior to starting any subsequent therapy (or infusion). If disease recurred, specify the first date of recurrence following the initial treatment and prior to starting additional therapy or infusion.

If CR was not achieved in response to the initial treatment plan, select **No**, the neuroblastoma did not recur.

If the exact date is not known, use the process for reporting estimated dates as described in the General Instructions, Guidelines for Completing Forms.

Question 180: Specify the date of the best response to chemotherapy was determined

Enter the date the best response to chemotherapy was established. This should be the earliest date all international working group criteria were met for the response reported above. Report the collection date of the first pathological evaluation, radiographic, or lab assessment (e.g., bone marrow biopsy, CT scan, urine studies, etc.). If no pathological, radiographic, or laboratory assessment was performed to establish the best response to the line of therapy, report the office visit in which the physician clinically assessed the recipient's response.

If the exact date is not known, use the process for reporting estimated dates as described in the General Instructions, Guidelines for Completing Forms.

If the date of best response was not known, select the **Date best response to chemotherapy was determined unknown**. This option should be used sparingly and only when an estimated date cannot be reported.

Question 181: Did the recipient undergo surgery, chemotherapy or other cytotoxic treatment for persistent or recurrent disease after the initial treatment but prior to the preparative regimen?

Indicate whether the recipient underwent surgery, chemotherapy or other cytotoxic treatment after the initial disease treatment but before the start of the preparative regimen / infusion.

Reporting Multiple Lines of therapy
Complete *Date therapy started* through *Date of relapse / progression* for each line of therapy administered for persistent or recurrent disease after the initial treatment and prior to the start of the preparative regimen (or prior to infusion if no preparative regimen was given). When submitting the paper version of the form for more than one line of therapy, copy the "Pre-HCT or Pre-Infusion Therapy" section and complete a copy of the section for each line of therapy administered.

Multiple Lines of Therapy
A single line of therapy refers to any agents administered during the same time period with the same intent (induction, consolidation, etc.). If a recipient's disease status changes resulting in a change to treatment, a new line of therapy should be reported. Additionally, if therapy is changed because a favorable disease response was not achieved, a new line of therapy should be reported. Refer to the Lines of Therapy reporting instruction overview for more information.

Question 182: Date therapy started

Enter the date the recipient first began this line of therapy.

If the exact date is not known (e.g. the recipient started in mid – July 2010), use the process for reporting estimated dates as described in the General Instructions, Guidelines for Completing Forms.

Question 183: Date therapy stopped

Enter the date of the final administration for the therapy reported. If the therapy is administered in cycles, report the date the last cycle started for this line of therapy.

If the exact date is not known (e.g. the recipient started in mid-July 2010), use the process for reporting estimated dates as described in the General Instructions, Guidelines for Completing Forms.

Question 184: Systemic therapy

Systemic therapy refers to a delivery mechanism where a therapeutic agent is delivered orally or intravenously to the whole body. These drugs enter the bloodstream and are distributed throughout the body.

Specify if the recipient received systemic therapy after the initial treatment plan as part of the reported line of therapy.

If it is not known if systemic therapy was given as part of the line of therapy being reported, select **No**.

Question 185: Number of cycles

Chemotherapy is usually administered in cycles with rest periods between the cycles. This enables cancer cells to be attacked at vulnerable times and provides healthy cells adequate time to recover from the damage. A cycle can last one or more days and may repeat weekly, bi-weekly, monthly, etc. A chemotherapy course may consist of multiple cycles.

Enter the number cycles the recipient received during this line of therapy being reported. If the therapy is not given in cycles or the number of cycles is not known, then check **Number of cycles unknown / not applicable**.

Questions 186 – 197: Treatment

For each drug, indicate if it was given as part of the line of therapy being reported. Do not leave any response blank.

If the recipient received an agent that is not listed, check **Yes** for the *Other therapy* and specify the treatment. Report the generic name and not the brand name.

Question 198: Radiation therapy

Radiation therapy uses high-energy, ionizing radiation to kill malignant cells. Much like non-targeted systemic therapy, radiation therapy does not specifically target malignant cells and does have significant side effects. For that reason, high-dose radiation often targets a limited field.

Indicate if the recipient received radiation therapy after the initial treatment as part of the line of therapy being reported.

If it is not known if radiation therapy was given as part of the line of therapy being reported, select **No**.

Questions 199 – 205: Specify the site(s) of radiation therapy

For each site, indicate if radiation therapy was given. If radiation was given specify the number of fractions administered to the site and the dose per fraction in centigrays (cGy / rads).

If radiation was given to a site not listed, select **Yes** for *Other site, and specify.*

Questions 206 – 207: Surgical biopsy / resection

Indicate if surgery was used to biopsy or resect all or a portion of the tumor tissue as part of the reported line of therapy.

If not known if surgery or a resection was not performed as part of the line of therapy, being reported, select **No**.

Question 208: Type of surgery

Specify the type of surgery performed (biopsy, partial, gross total, etc.).

- **Gross total:** > 95% resection, no radiographic residual tumor
- **Near total:** 90 – 95% resection, minimal radiographic residual tumor.
- **Subtotal:** 51 – 89% resection, moderate radiographic residual tumor.
- **Partial:** 10 – 50% resection, significant radiographic residual tumor. This method of approach is often used when there is a risk of neurological damage
- **Biopsy:** < 10 % resection, no radiographic change from pre-op. Usually preformed to be examined and confirm diagnosis.

Question 209: Histologic diagnosis

Neuroblastic tumors can be classified as ganglioneuroblastomas, ganglioneuromas, or neuroblastomas. These neuroblastic tumors differ histologically in degree of cellular and extracellular maturation. Ganglioneuroblastomas consist of mature gangliocytes and immature neuroblasts resulting in intermediate aggressive behavior. Ganglioneuroma is the most benign tumor of the three and exhibits greater degrees of maturation. Neuroblastoma is the most malignant and immature of the three tumors.

Indicate if the biopsied / resected tissue has the histological diagnosis of **Ganglioneuroblastoma**, **Ganglioneuroma**, or **Neuroblastoma**.

Question 210: Best response to line of therapy

Based on the International Neuroblastoma Response Criteria, specify the best response to the reported line of therapy. The best response is determined by a disease assessment, such as radiology or pathology and may occur during the therapy or after, but prior to starting the next treatment / infusion.

If the disease status was not reassessed prior to starting the next treatment or infusion, select **Unknown**.

Question 211: Date response evaluated

Enter the date the best response to chemotherapy was established. This should be the earliest date all international working group criteria were met for the response reported above. Report the collection date of the first pathological evaluation, radiographic, or lab assessment (e.g., bone marrow biopsy, CT scan, urine studies, etc.). If no pathological, radiographic, or lab assessment was performed to establish the best response to the line of therapy, report the office visit in which the physician clinically assessed the recipient's response.

If the date of best response is not known, use the process for reporting estimated dates as described in the General Instructions, Guidelines for Completing Forms.

Question 212: Did the patient relapse / progress following this line of therapy?

Indicate if relapse / progression occurred during the reported line of therapy or after, but prior to starting a new line of therapy / infusion. Refer to the Neuroblastoma Response Criteria section of the Forms Instructions Manual.

Question 213: Date of relapse / progression

Report the date of the first assessment that identified relapse or progression. The date the sample was collected for pathological / laboratory evaluation or the date the imaging took place should be reported. If the physician determined evidence of relapse in a clinical assessment during an office visit, report the date of clinic visit.

If the exact date is not known but can be estimated, then use the process for reporting estimated dates as described in the General Instructions, Guidelines for Completing Forms.

Sites of Tumor Involvement and Subsequent Infusions
For subsequent infusions, report sites between last the previous infusion and the preparative regimen for current infusion.

Questions 214 – 228: Specify any sites of tumor involvement at any time after diagnosis but prior to the preparative regimen

For each site, indicate if there was tumor involvement at any time after diagnosis but prior to the start of the preparative regimen / infusion. Do not leave any response blank.

If there was tumor involvement at a site not listed, indicate **Yes**, for *Other site* and specify the site.

Section Updates

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

Q229 – 261: Disease Status Immediately Prior to Preparative Regimen

Disease Assessments Prior to Preparative Regimen

All values reported below must reflect the most recent testing performed prior to the start of the preparative regimen (or infusion if no preparative regimen was given). Assessments performed during the last line of therapy or after the last lie of therapy may be reported. If multiple assessments were performed, report the most recent. If additional therapy was given after the last assessment, do not report the test.

Question 229: Were tumor marker analyses performed immediately prior to the preparative regimen?

Tumor markers, also known as biomarkers, are substances produced by cancer tissue or by the body in response to cancer at higher than normal levels. In certain situations, these substances can be used to detect and monitor disease due to their elevated presence in blood, urine, and/or tissue. The substances listed below have been identified as potential tumor markers for neuroblastoma.

Specify if tumor marker analyses were performed at the last evaluation prior to the start of the preparative regimen / infusion. If testing was not performed or unknown if performed, select **No**.

Questions 229 – 241: Specify the tumor marker analyses performed

For each tumor marker, indicate if it was analyzed at the last evaluation prior to the preparative regimen / infusion. If analyzed, select **Known** and specify the value. If the analysis was not performed or it is unknown if performed, select **Not known**.

- Homovanillic acid (HVA): Catecholamines (e.g. epinephrine/adrenaline) are secreted as hormones from the adrenal medulla. Neuroblastomas typically produce excessive levels of these catecholamines. After catecholamines are secreted they are broken down into metabolites including Homovanillic acid (HVA) and Vanillylmandelic acid (VMA). Both HVA and VMA are excreted in the urine. As a result, elevated levels of HVA and VMA detected by urinary analysis can be indicative of neuroblastoma.
- Neuron specific enolase (NSE): A glycolytic enzyme (enolase) specific to neuronal-type tissues. NSE may be excessively expressed by neuroblastomas and indicative of disease.
- Other tumor marker analysis: If testing for a tumor marker was performed at diagnosis and is not listed above, select **Known**, specify the tumor marker, value and units of measurements. Examples of other testing can include Chromogranin A (CgA) or Neuropeptide Y (NpY).

Question 242: Specify the total number of complete remissions

Report the total number of complete remissions (CR) achieved, including the most recent CR from diagnosis until the start of the preparative regimen / infusion.

For subsequent infusions, include all CRs achieved from the original diagnosis to the start of the preparative regimen for the current infusion.

Questions 243 – 260: Specify any known sites of disease immediately prior to the preparative regimen

For each site, indicate whether disease was identified at the last evaluation prior to the start of the preparative regimen / infusion.

If disease was present in the recipient's bone marrow immediately, indicate if bone marrow morphology, flow cytometry, and / or immunofluorescence was performed to evaluate the bone marrow at the last evaluation prior to the start of the preparative regimen / infusion.

If a site was known to have disease at the time immediately prior to the start of the preparative regimen and is not listed as an option, select **Yes**, for *Other site* and specify the site.

Question 261: Specify the percent of cells positive for neuroblastoma

Report the percent of cells positive for neuroblastoma from the site(s) reported above at the last evaluation prior to the start of the preparative regimen / infusion. If multiple sites were selected, the percentage of positive cells identified in the bone marrow should be reported.

Section Updates

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