

CMC IR 5.5.17

1. In section 3.2.S.2.1 (Manufacturer(s)) you indicate that the (b) (4) Vector will be stored at the (b) (4).
Please provide the following information:
 - a. Please provide an outline on how you will decide between (b) (4) the vector at the (b) (4) facility versus the (b) (4) facility.
 - b. Please provide details about the (b) (4) facility, how the vector will be stored and how the temperature will be monitored.
2. In section 3.2.S.3.1 (Characterization for (b) (4)) you indicate that (b) (4). Please provide details on how your (b) (4) assay was validated.
3. In section 3.2.S.3.2 (Impurities – (b) (4) Vector) you indicate that the analytical methods used to measure the (b) (4) were qualified at (b) (4). Please provide a copy of the (b) (4) protocol for (b) (4) determination and a description of the (b) (4) reference standards used.
4. In section 3.2.S.4.3 (Validation of Analytical Procedures - (b) (4) Vector; (b) (4)) you indicate that vector lot (b) (4) was used to evaluate repeatability and robustness to determine (b) (4) based on (b) (4) release. Please provide justification for the materials used in your validation studies, including the number of lots used. In addition, please provide (b) (4) assay results for vector manufacturing campaigns carried out at (b) (4) including campaigns (b) (4).
5. We note that apheresis centers will be providing collection bags containing the starting apheresis material, and that multiple types of collection device may be used. However, it is unclear whether more than one type of apheresis collection bag will be used. Please describe which apheresis collection bags will be used and provide container closure system information for each bag type, including manufacturer, description (including schematic diagram), identity of materials of construction, specifications, leachables and extractables information, and clearance type and number (if available).
6. Please describe which apheresis bags were used in the apheresis shipping and storage studies described in Section 3.2.S.2.2 Table 1 and Section 3.2.S.2.6. Please describe whether similar shipping and stability studies were conducted on other apheresis bags, and if so please provide details and data. If shipping and stability studies were not conducted on all of the apheresis bags to be used during commercial manufacturing, please provide a rationale for not conducting studies on all the bags to be used.
7. Please provide the following information regarding the (b) (4) used to contain the (b) (4) retroviral vector:
 - a. An assessment of extractables and leachables
 - b. An assessment of compatibility between the retroviral vector and the container
 - c. A description of any identification labels attached to the (b) (4) used for vector (b) (4)

8. Please provide information on the reference standards/positive controls used for the following lot release assays. Please include the source of the material, how it is characterized and the procedure for qualifying new material.
 - a. Cell viability
 - b. (b) (4)
 - c. Replication Competent Retrovirus (b) (4)
9. Please provide additional information on the axicabtagene ciloleucel lots being used as positive controls for the (b) (4) release assays including the site of their manufacture and the type of starting material.
10. Please provide information on the qualification scheme in place for the CD19 positive (b) (4) cells used for the (b) (4) release assay. Please include their source and how they are characterized prior to their use in the assay.