1. Regarding the (b) (4) ⬛⬛⬛⬛⬛⬛⬛⬛⬛ assay

    a. SOP TM-0009-QC3

        i. Please provide the (b) (4) ⬛⬛⬛⬛⬛⬛⬛⬛⬛⬛⬛⬛⬛⬛⬛⬛⬛⬛⬛⬛⬛ .

        ii. In P4.6, please provide the handling procedures for the reference (b) (4) ⬛⬛⬛⬛⬛

    b. Method Validation Report QR-0835

        (b) (4)

ix. For the assessment of robustness, please provide a justification for only assessing this quality using (b) (4) samples.

c. Method Transfer Report QR-0777

i. For the assessment of reproducibility, please indicate whether the samples used by both sites were prepared (extracted) at a single site and if so how they were transported to the receiving site.

2. Regarding the CD19 (b) (4) assay

a. SOP TM-0001-QC3

(b) (4)

b. Method Validation Report QR-0259

i. Please provide the following additional documents: SOP 0099, DR-00071, QR-0111, and the Amendment to QR-0111.

(b) (4)

c. Method Transfer Report QR-0579

(b) (4)

3. Regarding the (b) (4) and (b) (4) assay for axicabtagene ciloleucel

a. Method Validation Reports QR-0278 and QR-0521

(b) (4)

b. Method Transfer Report QR-0638

(b) (4)

(b) (4)

4. Regarding the (b) (4) assay for (b) (4)

   a. SOP TM-0022-QC3

      (b) (4)

   b. SOP TM-0023-QC3

      (b) (4)

   c. Method Validation Report QR-0788

      i. Please provide rationale for only assessing the precision (repeatability, intermediate precision) and robustness of this assay.

      ii. Please provide %CV acceptance criteria for the assay characteristics evaluated as part of the validation of this assay (repeatability, intermediate precision and robustness).

      iii. Please indicate whether this assay validation occurred at (b) (4) . Please be aware that assay validation must be conducted at the site where the assay will be conducted.

iv. Please provide data on the validation of the (b) (4) methods used as part of this assay.

5. Regarding SOP TM-0002-QC3 and SOP TM-0023-QC3

(b) (4)

6. Regarding Master Cell Bank Production (3.2.S.2.3 Control of Materials - (b) (4) Vector, Master Cell Bank Production): Please provide additional details on how the MCB clones were generated.

7. Regarding Working Cell Bank Stability (3.2.S.2.3 Control of Materials - (b) (4) Vector, Working Cell Bank Stability): Please provide a description of the (b) (4) testing to assess stability of the WCB. In addition please describe how you plan to measure functional activity of the WCB.

8. Regarding (b) (4) Data for PPQ Lots (3.2.S.2.5 Process Validation and/or Evaluation, Table 16, Impurity Data for PPQ Lots): (b) (4) . Please explain why an upper limit for (b) (4) values was chosen as an acceptance criteria rather than a lower limit.

9. Regarding Characterization and Storage Conditions of Reference Standards (3.2.S.5 Reference Standards or Materials ((b) (4)) (Establishment of Vector Positive Control Lot (b) (4) ; Characterization and Storage Conditions)): You indicate that the (b) (4) of this vector positive control (vPC) (b) (4) Please provide a plan on how stability of the vPC will be assessed beyond (b) (4) if you intend to use it for more than (b) (4)

10. Please consider testing for viability, anti-CD19 CAR expression, and potency by (b) (4) in addition to the tests for appearance and sterility performed on stability lots of donor-derived axicabtagene ciloleucel filled into the commercial container closure.

11. Please provide a proposed stability testing schedule for patient lots of axicabtagene ciloleucel filled into the commercial container closure.

12. Please describe how you intend to ensure that the cGMP grade (b) (4) is suitable for its intended use. In addition, please provide information on whether any animal derived components are used in manufacture or purification and whether any testing for adventitious agents is performed to qualify this material.

(b) (4)

(b) (4)