

From: Cagungun, Nannette  
Sent: Friday, July 21, 2017 4:11 PM  
To: Manisha.patel@novartis.com; narin.ahmed@novartis.com  
Cc: Giordano, Erica  
Subject: Information Request: Tisagenlecleucel -T

Importance: High

Our Reference: BL 125646/0

Dear Ms. Patel:

We are reviewing your February 2, 2017 biologics license application for Tisagenlecleucel -T for the treatment of pediatric and young adult patients with relapsed/refractory (r/r) B-cell acute lymphoblastic leukemia (ALL). We have reviewed your response (emailed to us on 7/19/2017) in regards to the analysis of (b) (4) tisagenlecleucel lot to support proposed lot release specifications. We have the following information request:

1. The proposed acceptance criteria for percentage of viable T cells is ? (b) (4) This limit is too low based on the beta distribution analysis and manufacturing experience. For the purpose of manufacturing a consistently pure product, please increase this criterion to ? (b) (4)
2. The proposed acceptance criteria for determination of transduction efficiency by CAR qPCR is (b) (4) (b) (4) copies/cell. Based on the data distribution and manufacturing experience, the proposed upper limit of (b) (4) copies/cell is too high. Please reduce the upper limit criterion to (b) (4) copies/cell.
3. The proposed acceptance criteria for release of IFN- ? in response to CD19-expressing target cells is (b) (4) IFN-?/transduced cell. The proposed upper limit of (b) (4) IFN-?/transduced cell is too high based on the beta distribution analysis, and we do not believe that it is justified to change this limit at this stage based on a single outlier data point. Please reduce this upper limit criterion to (b) (4) IFN-?/transduced cell.

Please submit the requested information in an amendment to the file by Tuesday, July 25, 2017, referencing the date of this request. If you anticipate you will not be able to respond by this date, please contact the Agency immediately so a new response date can be identified.

If you have any questions, please contact me at (240) 402-8267 or Ms. Erica Giordano at 240-402-8298.

Sincerely,  
Nannette Cagungun, MS, PD, RAC  
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Center for Biologics Evaluation and Research  
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