



Pioneering science delivers vital medicines™

Talimogene Laherparepvec Meeting

September 9, 2014

15:00 pm – 16:00 pm

List of Amgen Attendees

- Kathleen Sugrue-Richards, MS, Senior Manager, Regulatory Affairs, CMC
- Anne Marie Woodland, MS, RAC, Executive Director, Regulatory Affairs
- Tara Reed, MS, RAC, Senior Associate, Regulatory Affairs, CMC
- Paul J. Husak, PhD, Director, Product Quality
- Paul Bullock, PhD, Executive Director, Process Development
- David Hambly, PhD, Senior Scientist
- Allan Gibson, Director, Quality Control
- Colin Love, PhD, Vice President, Clinical Operations

Question 1a

Agency Question:

At this time we ask that you provide method protocols and validation reports for in vitro and in vivo adventitious virus testing. Please include volumes tested.

Amgen Response:

In vitro adventitious virus testing performed on (b) (4)

Amgen will provide a method summary which includes volumes tested. Amgen commits to providing qualification reports for the following:

- Contract lab validation reports for the in vitro (b) (4)
- Product qualification performed at the contract lab, including in vitro adventitious virus

In vivo adventitious virus testing performed on (b) (4)

(b) (4)

Amgen will provide a method summary which includes volumes tested. Validation of the in vivo adventitious virus (b) (4) is not typically performed. Due to the use of a (b) (4), Amgen performed an (b) (4) qualification which Amgen will provide.

Question 1b

Agency Question:

Please provide method descriptions (and validation reports) for (b) (4) and (b) (4) determination.

Amgen Response:

Amgen will provide a method description and validation report for (b) (4) determination of (b) (4) during the (b) (4) process.

(b) (4)

Question 1c

Agency Question:

Please provide verification reports for all compendial assays.

Amgen Response:

Amgen will provide verification reports for the following compendial assays:

- (b) (4)

| [REDACTED]

| [REDACTED]

| [REDACTED]

Visual methods (Color and Appearance) assess intrinsic physical properties for which there are no applicable method validation categories.

Compendia equivalent methods for (b) (4) [REDACTED] have system suitability criteria that ensure accuracy and precision.

Question 2a

Agency Question:

Provide a summary of risk assessment and analysis for process changes and production scale up.

Amgen Response:

Amgen has performed a risk assessment and analysis on the process changes leading into commercial production and will provide a summary to the Agency.

Amgen performed an analysis of the process changes associated with the process scale-up to the (b) (4) and will provide a summary.

Question 2b

Agency Question:

Provide a justification for the specification of (b) (4) listed as acceptable hold times for (b) (4) manufacture.

Amgen Response:

The (b) (4) manufacturing process is controlled to the validated (b) (4) times, which were established during process validation.

The acceptable hold times for (b) (4) manufacturing process were defined through characterization studies during process development. Representative in-process (b) (4) was held to end time points of (b) (4) and (b) (4) respectively. The study confirmed product stability as measured by (b) (4) over the duration of the acceptable hold time.

The validated hold times may be extended within, but not to exceed, the acceptable characterized hold times through additional validation.

Question 2c

Agency Question:

Detailed information on the external standards (example: For (b) (4) used in (b) (4) assays: information on purity, method of manufacture, source, and a sample certificate of analysis).

Amgen Response:

Amgen will provide the CoA for the following external standards. No other methods use external standards.

Assay	Control	Manufacturing Source	Vendor
(b) (4)			

Question 2c (continued)

Agency Question:

Detailed information on the external standards

Amgen Response:

Amgen will provide the CoA for the following external standards. No other methods use external standards.

Assay	Control	Manufacturing Source	Vendor
(b) (4)			