Amgen BLA 125518 DMPQ Manufacturing Site and FEI Teleconference

Date October 17, 2014
Time: 2:00pm

Meeting Minutes:

Primary Discussion Items:

1. *Registering for an FEI number.*

   Preliminary Response: Amgen would like to also understand the FDA's position on FEI and DUNS numbers used as facility identifiers supporting inspectional activities. For future applications, confirmation on whether a DUNS number is sufficient or if both DUNS and FEI numbers are required would be greatly appreciated.

   Meeting Discussion: DMPQ provided clarification that the DUNS number is used as a business identifying number but not as a registration number for establishment inspections. A FEI number is needed for all sites. This is across FDA, not CBER specific. DMPQ referred to the CDER drug registration site which provides instructions to electronic request for registration and FEI numbers.
   Actions: Amgen request FEI numbers for sites listed below: (b) (4) Abingdon, Woburn by Monday, October 20.
   Michelle Pernice will communicate to Mark Davidson if any further clarification is needed for this process.

Secondary Discussion Items:

2. *Indicate if the Amgen facility,* (b) (4) *) is a primary packaging or secondary packaging site.*

   Preliminary Response: The Amgen facility, (b) (4) is a secondary packaging site responsible for the following specific activities:

   Receives frozen labeled drug product (LDP); Stores frozen LDP; Packages frozen LDP into secondary carton at which time it is considered finished drug product (FDP); Stores frozen FDP; Distributes frozen FDP

   Meeting Discussion: DMPQ confirmed the information provided is sufficient.

3. *Indicate if the* (b) (4) *. sites in the* (b) (4) *listed in your BLA to perform drug product release and safety testing are located at the same site Amgen preliminary meeting comment/response:*

   Preliminary Response: There is not a single site that performs both DP release and safety testing. There are multiple (b) (4) test sites, which are used as back-up testing laboratories. Drug product release and safety testing primary and backup test site locations are outlined in Table 1 and detailed in Table 2 and Table 3 provided as part of the preliminary response to this meeting . (b) (4)

subcontractors (i.e., (b) (4))) operate as the primary test facilities for drug product release and safety testing.
(b) (4)) provide backup testing services for both drug product release and safety testing. As detailed in Table 2 and Table 3.

(b) (4)) is the primary test site for:
Endotoxin and *In vitro* testing for viral contaminants

(b) (4) subcontractor is the primary test site for: Sterility and (b) (4)

(b) (4) subcontractor is the primary test site for: *In vivo* testing for adventitious agents and Abnormal toxicity

(b) (4) is the backup test site for:
Endotoxin, Sterility, Abnormal toxicity, (b) (4) , *In vitro* testing for viral contaminants

(b) (4)) is the backup test site for:
In vivo testing for adventitious agents

Meeting Discussion: Amgen confirmed that all final product release testing is done at the Abingdon, UK facility with the exception of safety testing, which is performed at (b) (4) as backup for risk mitigation.
Actions: Amgen will confirm if the (b) (4) sites are in one site, one building? Or multiple buildings in one plaza?
***Post meeting note*:** Amgen confirms that the (b) (4) sites are located in the same industrial park but not in the same building

4. *Providing supporting validation/qualification data (HVAC, Equipment, Media fills) for the facilities and any facility changes as part of the BLA submission.*

Preliminary Response: Historical media fill data is provided in 3.2.P.3.5. Process Validation and Evaluation and includes a summary of the data from 2013 media fill runs. Amgen commits to provide the requested 2014 media fill data to support changes to the fill suite, as communicated in the RTQ submission submitted on Friday, October 10, 2014 (BLA 125518, SN 0003). Historical Equipment and facility qualification/validation technical reports including, HVAC, facilities and equipment qualification data will be readily available during the FDA's on-site prior approval inspection. In line with ICH eCTD guidelines Amgen has provided a description of the facility, utilities, equipment and operations that are conducted at the AWM facility within the appendices (3.2.A.1 Facilities and Equipment) section of the BLA.

Discussion: DMPQ informed Amgen that significant CMC information was not included in the BLA and referenced the following guidance documents that define the CMC information that should be included in a BLA submission.

"Guidance for Industry, Content and Format of Chemistry, Manufacturing and Controls Information and Establishment Description Information for a Vaccine or Related Product" and "Guidance for Industry for Submission Documentation for Sterilization Process Validation in Applications for Human and Veterinary Drug Products."

DMPQ acknowledged that Amgen followed the eCTD guidance for the information to provide in the BLA submission; however, informed Amgen that the two other guidance documents noted above are also applicable given that their product has similarity to a vaccine in regards to mode of action and in the manufacturing process, thus the CMC information outlined in these guidances relating to a vaccine should be followed. Amgen indicated that they are aware of these guidances and were expecting to provide all necessary information on inspection. DMPQ indicated that the information outlined in these guidances will also be checked on inspection; however, re-iteriterated that this information also needs to be part of the BLA file.

In regards to the facility changes, DMPQ asked Amgen when the filling suite changes were implemented and how many media fills have been performed that support the fill suite expansion. Amgen indicated that the facility fill suite expansion activities were completed at the beginning of Q3 2014. In addition, Amgen also indicated that Amgen Woburn shared a common building with a previous tenant and the tenant needed to move out before these construction activities could occur. In regards to the number of media fills performed, Amgen indicated that (b) (4) media fills have been performed and were completed this month. The testing for the media fills is currently ongoing.

DMPQ reminded Amgen that any late components to a PDUFA V application were to be discussed and agreed upon during the pre-BLA meeting. The filling suite modification and submission of supporting information for this modification was not discussed at this meeting or at any time before filing of the BLA. The supporting information should be submitted as soon as possible. The late submission of this information could be problematic.

Actions: DMPQ will send an information request to provide information needed to perform BLA review. Amgen will provide the requested data as soon as possible.

FDA Attendees:

Laurie Norwood
Christine Harman
Carolyn Renshaw
Nancy Waites
Ramjay Vatsan
Mark Davidson
Daniel Takefman

Amgen Attendees:

Laura Hill
Anne Marie Woodland
Tara Reed
Mike Abernathy
Michelle Pernice
Amanda Kennedy