Dawn M. Viveash, M.D.
Vice President
Global Regulatory Affairs & Safety

AMGEN

Amgen
One Amgen Center Drive
Thousand Oaks CA 91320-1799
805 447.1000
Direct Dial: 805 447 6203
E-mail viveashd@amgen.com

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Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, RM 1061
Rockville, MD 20852

Reference: **Docket No. 2003D-0382**
Draft Guidance for Industry on Sterile Drug Products Produced by Aseptic Processing

Amgen is pleased to provide comments on the FDA Draft Guidance for Industry on Sterile Drug Products Produced by Aseptic Processing. Amgen acknowledges the FDA's effort in the publication of this document, which provides additional guidance from the previous version, considers advances in technology, and recognizes industry best practices.

Our comments are intended to further strengthen the document. We believe that our comments are aligned with current industry practice and are based on sound scientific and practical rationale.

These comments include references to two sections of the document that require measuring or monitoring that would not provide meaningful data. The first is measuring the airflow velocity at the work surface (Line 331), and the second is monitoring critical surfaces for microbial contamination (line 1152). Each of these activities could result in inconsistent or questionable data due to the potential adverse effect of the activities themselves.

An additional comment is in regards to air change rates for specified room classifications (Line 249). While we are well aware that air changes are indirectly related to the quality of air, the guidance provides for a "typically acceptable" rate, which is unnecessarily prescriptive. The room air quality requirements, as per current regulation, related to viable and non-viable particulate, HEPA face velocity, and room differential pressures will drive the need to adjust the air supply and return volumes until these requirements are achieved. Thus, air changes should not be a requirement.

The final comment is in response to the statement that the final dosage form manufacturer is responsible for review and approval of validation documents for contract manufacturers performing sterilization/depyrogenation of containers and closures (Line 623). This is an unnecessary requirement and is not a typical industry practice. Assessing compliance to "the same cGMP requirements as those established for in-house processing" for a contract

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One Amgen Center Drive
Thousand Oaks, CA 91320-1799
805.447 1000
Direct Dial: 805 447.6203
E-mail vivcashd@amgen com

manufacturer or supplier can be accomplished through a supplier quality or contract manufacturers auditing program.

Amgen appreciates the opportunity to comment on this draft guidance. If you require further information, please feel free to contact me at (805) 447-6203 or viveashd@amgen.com.

Sincerely,

Dawn Viveash
Vice President,
Regulatory Affairs

Attachment

Comments on FDA Draft Guidance on Sterile Drug Products Produced by Aseptic Processing

Line Ref.	Comments
249	**Text:** "For Class 100,000 (ISO 8) supporting rooms, airflow sufficient to achieve at least 20 air changes per hour would be typically acceptable. For areas of higher air cleanliness, significantly higher air change rates will provide an increased level of air purification." **Comment:** Delete the unnecessary specificity for air changes per hour. **Rationale:** Air quality requirements, i.e. viable, non-viable, HEPA certifications, HEPA face velocity and differential pressures will drive the necessary adjustments needed in air supply and return to achieve these requirements. If the manufacturer is meeting these requirements and demonstrating unidirectional airflow at the work surface, there is no need to comply with a fixed air change value.
331	**Text:** "Airflow velocities are measured 6 inches from the filter face and at a defined distance proximal to the work surface for HEPA filters in the critical area." **Comment:** Air velocity should be measured at the filter face only and not the work surface. **Rationale:** An acceptable airflow visualization study (smoke study) showing unidirectional flow from the top of the room to the working level is more relevant than the velocity measurements at the work surface. These measurements can be distorted by equipment, adjacent equipment configurations at the point of measurement, and other factors. Thus, more turbulence could be created and result in inconsistent data.

Comments on FDA Draft Guidance on Sterile Drug Products Produced by Aseptic Processing (continued)

Line Ref.	Comments
623	**Text:** "The finished dosage form manufacturer is responsible for the review and approval of the contractor's validation protocol and final validation report". **Comment:** This is an unnecessary requirement. **Rationale:** The finished dosage form manufacturer audits contract facilities that perform sterilization and/or depyrogenation of containers and closures as well as suppliers of sterile container and closure components. Audits are performed at an established frequency to assure compliance to cGMP requirements.
1152	**Text:** "The monitoring program should cover all production shifts and include air, floor, walls, and equipment surfaces, including the critical surfaces that come into contact with the product, container, and closures". **Comment:** Monitoring of sterile surfaces does not necessarily provide meaningful information. **Rationale:** There is a good probability that these surfaces (e.g., filling needles, stopper bowl) could be contaminated by the act of sampling itself. Even negative results may not be meaningful given that recovery efficacy is not 100%. In fact, the media fill exercise, with appropriate intervention challenges, will provide more meaningful data than actual sampling. Media fill data would confirm the viable condition of product contact surfaces and those surfaces in contact with containers and closures.