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Date: ▶ March 8, 2004

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

Ref.: [Docket No. 2003D-0493]

Draft Guidance for Industry – Powder Blends and Finished Dosage Unit – Stratified In-Process Dosage Unit Sampling and Assessment

Dear Sir/Madam:

Amgen Inc. is pleased to provide these comments on the Draft Guidance for Industry on Powder Blends and Finished Dosage Unit – Stratified In-Process Dosage Unit Sampling and Assessment. Amgen Inc. is a global biotechnology and pharmaceuticals products company based in Thousand Oaks, CA.

Comments:

Point #1

Predict In-Process Dosage Form Uniformity When RSD of Blend Sample is Smaller Than 3%

In accordance with PQRI datamining, blend uniformity (BU) data is predictive of final dosage form uniformity when blend RSD is less than 3% (Ref 1). Content Uniformity (CU) is highly correlated with Blend Uniformity. Therefore, if development data showed consistent BU with RSD less than 3%, the proposed stratified sampling plan for exhibit and/or process validation batches (e.g., 3 replicate samples per location from 20 locations) could be reduced to fewer samples/locations.

Point #2

Choice of Sampling Plans When Total RSD Is Smaller Than 3%

In accordance with the Final PQRI Blend Uniformity Working Group Recommendation (Figure 2, Between Location Variability Exists- Ref 2), the “20x3, 7” sampling plan and USP content uniformity test method for tablets are compared for increasing total variability (between location RSD varies from 1-10%, while maintaining the % RSD values for both weight variation and assay each at 1.5%). As the total RSD is smaller than 3%, the two sampling plans give the same close to 100% probability of meeting acceptable criteria. Therefore, if the BU and CU RSDs are less than 3% in demonstration batches, it should be sufficient to only test the CU of the final product without testing blend or stratified samples in routine manufacturing.

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Point #3

Apply the Guidance to Approved Products

There is a lack of guideline on how extensive the Stratified In-Process Dosage Unit Sampling as specified in this Guidance should be applied to already approved products. For example, existing data from demonstration batches should be used to determine what criteria of routine testing to use without generating new data.

If you have any questions regarding our comments, or how we may assist with further development of the Guidance, please contact me.

Sincerely,



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REFERENCES

1. Product Quality Research Institute /Blend Uniformity Working Group (PQRI/BUWG). Datamining. *Results of PQRI Datamining Effort*, Report slides prepared by Tom Garcia (Chair, PQRI/BUWG). December 12, 2001.
http://www.fda.gov/ohrms/dockets/ac/01/slides/3804s1_06_garcia-boehm/sld048.htm
http://www.fda.gov/ohrms/dockets/ac/01/slides/3804s1_06_garcia-boehm/sld045.htm
2. Product Quality Research Institute /Blend Uniformity Working Group (PQRI/BUWG). December 31, 2002. Final Blend Uniformity Recommendation: *The Use of Stratified Sampling of Blend and Dosage Units to Demonstrate Adequacy of Mix for Powder Blends*. <http://www.pqri.org/datamining/imagespdfs/011003rec.pdf>