

March 4, 2004

Eli Lilly's Response to [Docket No. 2003-0493] Draft GUIDANCE FOR INDUSTRY--- Powder Blends and Finished Dosage Units---Stratified In-Process Dosage Unit Sampling and Assessment

INTRODUCTION

Eli Lilly and Company has completed a thorough review of the Draft Guidance for Industry on Powder Blends and Finished Dosage Units—Stratified In-Process Dosage Unit Sampling and Assessment; Assessment, issued by the Food and Drug Administration under docket No 2003D-0493. Lilly has a few general areas of comment with regards to this proposal.

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MAJOR COMMENTS ON DRAFT GUIDANCE

This guidance provides a new approach for ensuring compliance to the GMP 21 CFR 211.110(a)(3), which Lilly and other companies have historically controlled through development, blend uniformity validation, and routine monitoring of dosage units and in-process weight control. We believe that this is an important guidance because it provides a new systematic approach for demonstrating blend uniformity when implementation of process analytical technology (PAT) is impractical or not possible.

One area of concern is the timing allowed for manufacturers to meet the requirements of this guidance document. Numerous activities may need to be identified and implemented to be compliant with this guidance. Activities include stratified sampling, testing, training, revision of SOPs and manufacturing documents, and evaluation of data. In consideration of the above, Lilly believes a transition period (e.g. eighteen months) should be provided for in the guidance.

Finally, the scope of the guidance is broader than what was discussed by PQRI in that it includes products that would currently be controlled by USP Weight Variation. This would include “products containing 50 mg or more of an active ingredient comprising 50% or more, by weight, of the dosage unit or, in the case of hard capsules, the capsule content”¹. For drug products which fall into this USP category, we believe analytical

¹ 2004 USP vol 27, p2396

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testing of the dosage units is unnecessary and would negatively offset the cost savings expected from this proposal as a whole.

PROCESS FEEDBACK

Lilly found the PQRI forum to be a very efficient and effective way to generate a strong working proposal on blend uniformity. As a result of the participation by topic leaders in the FDA, academia, and industry a draft recommendation, based on solid science and public feedback, was submitted to the Agency.

Since the process of working with PQRI was so successful, Lilly supports the use of the PQRI committee to work through other technical regulatory issues in the future.

EDITORIAL SUGGESTIONS

The basic concepts and approach in this guidance document are viewed by Lilly as sound and based on good science. While the overall flow and verbage in the document are acceptable, Lilly has provided a number of editorial suggestions to this document, which we believe will enhance the understanding, clarity, and flow of the document. These editorial suggestions do not change the document's content. Three appendices are included in helping understand the editorial suggestions.

- Appendix A This is the original Guidance with tracked (highlighted) editorial suggestions.
- Appendix B A matrix with rationale for each of the editorial suggestions.
- Appendix C A clean copy of the Guidance with the incorporated suggestions for ease of reading



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