

Item C: Implementation of Regulatory Flexibility (reference Line 98)

The guidance discusses and offers the concept of regulatory flexibility with respect to implementing changes. There is no discussion as to how these changes will be implemented. Implementation can occur through several means such as a supplement, a comparability protocol, or implementation through the firm's own quality system. Firms committed to investing the time and resources to implement a quality systems approach should be able to realize the benefits of regulatory flexibility. This guidance is not the place for this amount of detail, however, the Agency should prioritize the development of further guidance on this critical topic.

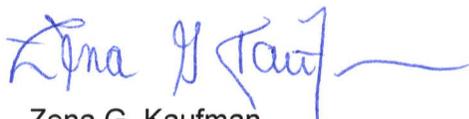
Item D: Active Pharmaceutical Ingredients (line 116)

Components (§ 210.3) are defined as any ingredient intended for use in the manufacture of a drug product. This guidance states the application of this guidance may be useful to manufacturers of components. Specific to the manufacture of Active Pharmaceutical Ingredients, there should be acknowledgement that by implementing a quality systems approach, API manufacturers can also take advantage of the regulatory flexibility discussed in lines 98 through 103. For manufacturers of components, other than Active Pharmaceutical Ingredients, implementation of this guidance should be optional and risk based.

Item E: Linkage to the Pharmaceutical Inspectorate (reference line 290)

Two of the key achievements of the FDA GMP Initiative are the development of the Pharmaceutical Inspectorate and the PATRIOT team. The PATRIOT team has provided cross functional training for defined inspectors who will be using the guidance during inspections. In an analogous manner, inspectors will need to be able to assess the application of principles within this guidance falling outside of regulatory requirements. These inspectors will need to be able to evaluate application of risk management processes transferring between what is required within the regulations and what is interpreted as current GMPs. Inspections must still be grounded in the actual regulations. The agency should give careful consideration to how to incorporate risk management and other optional practices into the pharmaceutical inspectorate curriculum.

Sincerely,



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