Considerations for the “Two for One” Inspection:
Assessing Application Approvability and cGMP Compliance in a Single Inspection

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A Tool for Assessing cGMP Compliance

For manufacturer inspections, the authority to inspect extends to:

...all things therein (including records, files, papers, processes, controls, and facilities) bearing on whether prescription drugs ... which are **adulterated or misbranded** within the meaning of this chapter, or which may not be manufactured, introduced into interstate commerce, or sold, or offered for sale by reason of any provision of this chapter, have been or are being manufactured, processed, packed, transported, or held in any such place, or **otherwise bearing on violation** of this chapter.

Objectives of Routine cGMP Inspections

- Determine whether inspected firms operate in compliance with cGMP requirements; if not, provide evidence for enforcement actions
- Support determination of acceptability of a firm’s new drug application
- Provide input to firms regarding cGMP compliance
- Further FDA’s expertise to guide assessments of cGMP requirements, regulatory policy and guidance documents

Enforcement – Stakes are High

- Inspectional Observations – Issuance of FDA Form 483
- Advisory/Administrative Action:
  - Warning Letter
  - Import Alert
  - Withhold NDA Approval

- Judicial Action
  - Seizure
  - Injunction
  - Prosecution
Ground for refusing an application:

- the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug:

  ✓ are inadequate to preserve its identity, strength, quality, and purity

  ✓ do not comply with the current good manufacturing practice regulations

cGMP Assessment vs. Review

**cGMP Assessment**

*Can the firm manufacture the product in conformance to the Application?*

**Review**

*What methods are adequate to preserve the drug’s identity, strength, quality, and purity?*
Combining cGMP compliance and application review

Potential to get safe and effective products to patients faster and more efficiently
Combining cGMP compliance and application review

- Company inspection management process must be aligned to serve additional purpose of inspection
  - Additional Subject Matter Experts Required
  - Increased flexibility for information requests
Combining cGMP compliance and application review

- 483s and Warning Letters – appropriate for findings related to application review?

- Jurisdictional questions for products not commercialized in U.S.?
INDUSTRY & FDA COLLABORATION WILL BE CRITICAL FOR SUCCESS!