PDA Comments on FDA Draft Guidance:

Circumstances that constitute delaying, denying, limiting, or refusing a drug inspection

July 12, 2013

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Background on FDASIA (FDA Safety and Innovation Act)

- In July 9, 2012 FDASIA was approved to allow FDA to:
  - Increase stakeholder involvement
  - Promote innovation
  - Collect user fees
  - Ultimately enhance safety of the drug supply chain
- Amends and/or adds to the Federal Food, Drug, and Cosmetic Act (FD&C Act)

http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/FDASIA/ucm20027187.htm

Primary Elements of FDASIA

Enhancing Supply Chain Safety
- Proposed Rule: Administrative Detention
- **Draft Guidance: Delay, Deny, Limit, or Refuse Inspections**
- Supply Chain Protection

Innovation Enhancements
- Breakthrough Therapy Designation
- Accelerated Approval Reforms

User Fees
- PDUFA V
- MDUFA III
- GDUFA (I)
- BsUFA (I)

Elements of FDASIA - Stakeholder

Sec. 905 of FDASIA

"The Secretary shall implement a structured risk-benefit assessment framework in the new drug approval process to facilitate the balanced consideration of benefits and risks, a consistent and systematic approach to the discussion and regulatory decision making, and the communication of the benefits and risks of new drugs.

Nothing in the preceding sentence shall alter the criteria for evaluating an application for premarket approval of a drug."

Mark Walderhaug, PhD , PDA/FDA Joint Regulatory Conference 2013

FDASIA's Impact on Drug Supply Chain

Drug Supply Chain – Inspections and Compliance Impacts

- New Unique Facility Identifier (UFI) system mandated including importers
  - Annual registration to be limited to 1 October to 31 December
  - Good Importation Practices (GIP) by 9 July 2015
    - Non-compliance leads to de-registration
- Mutual recognition of foreign inspections authorized
- Information sharing with foreign government authorized
  - FOI exemption for information received from foreign governments
  - FDA info only shared after certification that foreign government can maintain trade secret info control

John Finkbohner, PDA /FDA Joint Regulatory Conference, 2013

Drug Supply Chain – Highlights

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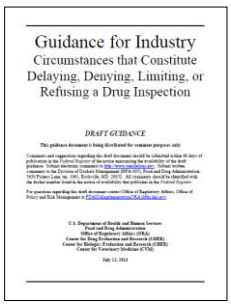
In support of FDASIA, FDA issued Draft Guidance in July 2013

- Section 704(a) of the FD&C Act provides FDA authority for inspections
- Section 706 of FDASIA amended section 704(a) of the FD&C Act by 49 allowing FDA to request, in advance of or in lieu of an inspection, within a reasonable timeframe, within reasonable limits, and in a reasonable manner, any records or information that 51 FDA may inspect under section 704(a).
- New section 501(j) of the 56 FD&C Act, as added by FDASIA section 707, now deems a drug to be adulterated if "…it has 57 been manufactured, processed, packed, or held in any factory, warehouse, or establishment and 58 the owner, operator, or agent of such factory, warehouse, or establishment delays, denies, or 59 limits an inspection, or refuses to permit entry or inspection."


Guidance for Industry

Circumstances that Constitute Delaying, Denying, Limiting, or Refusing a Drug Inspection

DRAFT GUIDANCE

Drug Supply Chain – Inspections Impacts

- FDA authorized to conduct joint investigations and notify foreign governments public health concerns
- FDASIA grants FDA "extraterritorial jurisdiction" over violations of FDCA for any article intended for import
  - Retained at POE may be destroyed without opportunity for export
- FDASIA expands FDA inspection authority on compelling record access
  - May require manufacturer to provide (*in advance or in lieu of inspection*) any records or information to FDA that the Agency may otherwise inspect at the facility (*either electronic or physical form*)

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FDA Draft Guidance - Comments

- In August of 2013 PDA drafted comments to:
  - *FDA Draft Guidance: Circumstances That Constitute Delaying, Denying, Limiting, or Refusing a Drug Inspection*
  - Comments developed by a PDA Task Force
  - Comments were reviewed and approved by the PDA Regulatory Affairs and Quality Advisory Board (RAQAB) and the Board of Directors
- The final PDA Comments were submitted in September 2013 to the FDA

PDA General Response to the FDA Draft Guidance

- FDA should provide a secure electronic system to receive inspection documents similar to the system for receiving electronic submissions for review.
  - Primarily to ensure/facilitate timely, secure document delivery from companies globally
  - The interpretation of a reasonable time frame may vary from one investigator to another and this should be taken under consideration
- Records in FDA possession must be secured as proprietary and confidential company information within the manufacturing documents being shared

Specific PDA Comments

PDA recommends:

FDA to provide additional clarification in this guidance regarding the interactions between firms and the agency if documents are requested in lieu of an inspection.

- How will companies be informed of any FDA concerns and allowed to respond during the inspection process?
- Will 483's be issued as a result of a paper inspection?

PDAs Recommendations for Clarification Text (1)

- After Line 79 of the FDA Draft Guidance**:** FDA will make reasonable accommodations for… *security situations, holidays, and other non-work days, and scheduled manufacturing campaigns.*, add the following thought:
  - **PDA: "During FDA international inspections, if documents are requested in English but are provided in a local language only, this will not be considered a delay of or refusal of the inspection. Companies may provide documents in English as a courtesy to the inspector."**

PDAs Recommendations for Clarification Text (2)

- Lines 125-129 of the FDA Draft Guidance**:** During and inspection……FDA requests records…but the *facility fails to produce the requested records within the timeframe requested by FDA, without adequate justification.*
  - **PDA: "Response time for specific situations may be negotiated between FDA and the company depending on the urgency and nature of the request, volume of the records requested, and logistical considerations such as geographical location of the records."**

PDAs Recommendations for Clarification Text (3)

- Lines 145-146 of the FDA Draft Guidance**:** *A facility does not allow the FDA investigator to inspect the facility by falsely alleging the facility does not manufacture drugs.*
  - **PDA: "It is acceptable for a company to refuse inspection, if it can provide documentation that manufacturing no longer occurs at this site and that no product manufactured at that site is still in distribution within the United States."**

PDAs Recommendations for Clarification Text (3)

- **Footnote [5] of the FDA Draft Guidance:** An unreasonable redaction is one that removes or obscures information that FDA is entitled to inspect by law. If the redaction does not obscure information over which FDA has no inspectional authority it generally will be considered reasonable. Section 704 (21 U.S.C. 374) states that FDA's inspectional authority does not extend to the following types of records: "financial data, sales data other than shipment data, pricing data, personnel data (other than data as to qualification of technical and professional personnel performing functions subject to this chapter), and research data (other than data relating to new drugs, antibiotic drugs, devices, and tobacco products and subject to reporting and inspection under regulations lawfully issued pursuant to section 355 (i) or (k) of this title, section 360i of this title, section 360j(g) of this title, or subchapter IX and data relating to other drugs, devices, or tobacco products which in the case of a new drug would be subject to reporting or inspection under lawful regulations issued pursuant to section 355(j) of this title)."

  - **PDA: "FDA's inspectional authority also does not extend to confidential internal audits."**

PDAs Recommendations for Clarification Text (4)

- Lines 177-180 of the FDA Draft Guidance**:** *Not allowing photography by an FDA investigator may be considered a limitation if such photographs are determined by the investigator(s) to be necessary to effectively conduct that particular inspection.*

  - **PDA: "FDA agrees not to take photographs in areas where photography is restricted by company policy or in areas where restrictions on photography are posted by the company."**

More information can also be found in the *IPQ Newsletter*

- Posted September 29, 2013
- www.ipqpubs.com
- Summary of PDA Inspection Trends Interest Group held at the PDA/FDA Joint Regulatory Conference, September 2013
- Includes summary of presentation by and discussion with FDA Baltimore District Pre-Approval Manager Brooke Higgins

Questions or Comments

आपका ध्यान के लिए धन्यवाद

Please tell your colleagues about our upcoming meeting in December!