PDA
Parenteral Drug Association

Connecting People, Science and Regulation®

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

Reference: FDA Draft Guidance for Industry Circumstances that Constitute Delaying, Denying, Limiting, or Refusing a Drug Inspection

Dear Sir/Madam,
PDA appreciates the opportunity to comment on this draft guidance which strengthens the FDA's ability to conduct necessary inspections to ensure manufacturing site are in conformance with GMPs.

Because this guidance includes the possibility of FDA requesting documentation in advance or in lieu of inspections, PDA suggests that FDA provide a secure electronic system to receive these documents comparable to the system for receiving electronic submissions. PDA also notes there is nothing in the guidance discussing company and FDA interactions if documents are requested in lieu of an inspection. PDA recommends FDA provide additional clarification in this guidance such as whether a 483 would be issued and how the company, who is the subject of the inspection, is given the opportunity to respond to any FDA questions or concerns when an inspection is conducted by review of submitted documentation.

PDA also suggests FDA provide clarification that response times for records requests may be negotiated depending on the urgency and nature of the request, volume of the records requested, and logistical considerations.

PDA is a non-profit international professional association of more than 10,000 individual member scientists having an interest in the fields of pharmaceutical, biological, and device manufacturing and quality. Our comments were prepared by a committee of experts with experience in pharmaceutical manufacturing and GMPs on behalf of our Regulatory Affairs and Quality Advisory Board and Board of Directors.

If there are any questions, please do not hesitate to contact me.

Sincerely,

Richard Johnson
President, PDA

CC: Rich Levy, PDA; Denyse Baker, PDA

Circumstances That Constitute Delaying, Denying, Limiting, or Refusing a Drug Inspection
Food and Drug Administration Draft Guidance
Sept 13, 2013

General Comments	Rationale
FDA should provide a secure electronic system to receive inspection documents comparable to the system for receiving electronic submissions for review. Records in FDA possession must be secured as proprietary and confidential company information.	It can be reasonably expected based on this guidance that FDA will increase their requests for documents in lieu of inspections. FDA should have a system in place to maintain security of any documents requested. Manufacturing documents contain company proprietary and confidential information that must be secured.
PDA recommends FDA provide additional clarification in this guidance regarding the interactions between firms and the agency if documents are requested in lieu of an inspection. Some outstanding question are: 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?	Inspections conducted remotely or via documents only should not preclude a company's ability to respond to concerns or clarify information with the inspectors in a timely way.

Line No.	Current Text	Proposed Change	Rationale
Section III	*New text to be added at the end of line 79*	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.	SOPs, batch records, validation documents, etc. written in a language not spoken by local employees in facilities inspected by FDA abroad would be a violation of cGMPs.
Foot note 5	*Section 704 (21 USC 374) states that FDA's inspectional authority does not extend to the following types of records…of this title).*	Add the following sentence: FDA's inspectional authority also does not extend to confidential internal audits.	Need to clearly state that FDA will not review or copy reports and records that result from internal audits under the written Quality Assurance Program per FDA Compliance Guide, CPG 130.300, last revised on June 2, 2007 and FDA Investigations Operations Manual for medical devices 5.6.2.2 Also reference is made to preamble to the Device QS/GMP .

125-129	*… the facility fails to produce the requested records within the timeframe requested by FDA, without adequate justification.* *• FDA requests records pursuant to section 704(a)(4) of the FD&C Act, but the facility fails to produce the requested records in a timely manner, without adequate justification.*	PDA suggests that FDA allow flexibility through dialogue between inspectors and the firmsby adding the following text. *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.*	The interpretation of a reasonable time frame may vary from one investigator to another. PDA would like to ensure that firms are allowed adequate response time when circumstances warrant.
145-146	*A facility does not allow the FDA investigator to inspect the facility by falsely alleging the facility does not manufacture drugs.*	Add this sentence: "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. "	Time and resources should not be wasted if facility is no longer manufacturing the drug which is the subject of the inspection.
161	*This includes the denial to disclose or permit observation of the manufacturing processes.*	Add the following sentence: "This assumes that limitations on room entry based on Environmental Health and Safety issues or other reasons such as gowning qualification for entry into the aseptic core must be considered. "	Circumstances when access is restricted should be clear and not perceived as limiting access to an inspector. Manufacturer should be allowed to provide clarity regarding specific situations when access limitations are warranted.
177-180	*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.*	Add the following sentence: "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."	Introduction of phtographic equipment into certain manufacturing areas may adversely impact ability to maintain control over the production environment or may compromise protection of proprietary technology therefore, firms may establish policies defining areas where photography is not permitted. As noted in FDA's Inspection Manual: Most legal experts agree that cases cited by FDA that provide authority to take photographs have not affirmed the agency's ability to take photographs in a facility which has a strict

			policy against photography and does not consent to the photography.
218-219	*…agent does not take steps to permit an inspection of a factory, warehouse, or other facility.*	add the following sentence: "Limitations on room entry based on Environmental Health and Safety issues or other reasons such as gowning qualification for entry into the aseptic core must be considered.	Circumstances when entry is restricted should be clear, defined in company policy or procedure, and not perceived as refusing entry to an inspector. Manufacturer should be allowed to provide clarity regarding specific situations when entry into certain areas of a facility is warranted.