FDA Issues Final Guidance Defining Circumstances that Constitute Delaying, Denying, Limiting or Refusing a Drug Inspection

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Under the Food and Drug Administration Safety and Innovation Act (FDASIA), enacted in 2012, a drug is adulterated if it "has been manufactured, processed, packed, or held in any factory, warehouse, or establishment and the owner, operator, or agent of such factory, warehouse, or establishment delays, denies, or limits an inspection, or refuses to permit entry or inspection." On October 22, 2014, the Food and Drug Administration published a *Federal Register* notice announcing a new final Guidance for Industry, "Circumstances that Constitute Delaying, Denying, Limiting, or Refusing a Drug Inspection," that defines several acts that it considers to be delaying, denying, or limiting an inspection, or refusing to permit entry or inspection.[1] While the guidance is limited to drug inspections, FDA might expand the guidance in the future to apply to other product areas, such as food, cosmetic or medical device companies.

Overview of Guidance

As described below, the guidance includes several examples that might lead to an FDA finding that a drug is adulterated. Many of these examples involve an action, or inaction, coupled with a lack of a "reasonable explanation" provided to the FDA inspector. While there are a few examples of potentially "reasonable explanations" described, the guidance does not provide a general definition of the phrase.

(1) Delays in scheduling pre-announced inspections: FDA explains that although it is not required to pre-announce its inspections, it often contacts a firm before an inspector arrives at the site. The agency may deem a drug to be adulterated if there is a delay in scheduling a pre-announced inspection, such as:

- a facility not agreeing to a proposed inspection start date and not giving a reasonable explanation for its failure to do so;
- a facility requesting a later start date after scheduling an inspection, without giving a reasonable explanation; and
- a facility failing to respond to FDA's attempt to contact the facility's designated contact.

(2) Delays during inspections: An inspection may be considered delayed if a facility's owner, operator, or agent engages in activities before or after the beginning of an inspection that interfere with the inspector's ability to perform the inspection. Examples of such activities include:

- a facility not giving access to an area of the facility until a specific future date or time, even though the area is operational and is in an area of the inspection site where FDA has the authority to inspect, without providing a reasonable explanation;
- a facility leaving the FDA inspector in a conference room and not providing timely access to necessary documentation or responsible individuals, thereby interfering with the inspector's ability to complete the inspection.

1 The guidance is available at: http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM360484.pdf

(3) Delays in producing records: When the FDA inspector requests records, which the agency is authorized to review, but the facility fails to produce the requested records in a timely manner and does not provide a reasonable explanation, FDA will classify such conduct as a delay in producing records.

(4) Denials of inspections: FDA may consider a drug to be adulterated if an owner, operator, or agent of a drug facility engages in an action or makes a statement that prevents an authorized agency representative from conducting or completing an inspection, such as:

- rejecting FDA's attempt to schedule a pre-announced inspection;
- not permitting the FDA employee to begin the inspection upon arrival;
- not allowing the FDA investigator to inspect the facility because certain staff members are not present, without providing a reasonable explanation;
- not allowing an inspection by falsely alleging that the facility does not manufacture, process, pack or hold drugs; and
- sending staff home for the day and telling FDA that the facility is not producing any product.

(5) Limiting access to facilities and/or manufacturing processes: FDA may deem a drug to be adulterated if an owner, operator, or agent of a drug facility prevents an inspector from having reasonable access to an area of the site that the agency is entitled to inspect through activities, such as:

- a facility ordering the discontinuation of all manufacturing for the duration of the FDA inspection without reasonable explanation;
- a facility imposing an unreasonably short time limit on the amount of time that the FDA inspector may directly observe the manufacturing process, in whole or in part;
- a facility limiting the direct observation of portions of the manufacturing process without reasonable explanation;
- a facility unreasonably restricting entry to a particular portion of the facility without reasonable explanation; and
- staff at a facility causing the FDA employee to leave the premises before the investigation is complete.

(6) Limiting photography: FDA may consider a drug to be adulterated if a drug facility impedes or resists photography by an FDA inspector who determines that the photographs are necessary to effectively conduct the inspection, and the facility does not provide a reasonable explanation for its activity. An example of a potentially reasonable explanation for limiting photography is that, due to the chemical properties of a product, taking photographs would adversely affect the quality of the product.

(7) Limiting access to or copying of records: FDA may consider a drug to be adulterated if a facility does not permit an authorized agency representative to have access to or copy records that the FDA is entitled to inspect by engaging in activities, such as:

- refusing to allow a review of the facility's shipping records;
- providing some, but not all, of the records requested by the FDA inspector; and
- providing records that are unreasonably redacted.

(8) Limiting or preventing the collection of samples: FDA may deem a drug to be adulterated if a facility prevents an authorized agency representative from collecting statutorily authorized samples, such as environmental samples, finished product samples, raw material samples, in-process material samples, and reserve samples in bioequivalence and bioanalytical studies.

(9) Refusing to permit entry or inspection: FDA may consider a drug to be adulterated if a facility owner engages in behavior (or non-action) that results in the inability to enter or fully inspect the facility. Examples of such action or inaction include:

- without reasonable explanation, barring the FDA inspector from entering the facility or certain areas of the facility by not unlocking the areas or taking other actions necessary to provide access;
- failing to respond to FDA's attempts to contact the facility's designated contact(s) to schedule an inspection; and
- failing to answer calls from the FDA employee who is present at the facility, despite clear evidence of the presence of employees engaged in job-related functions.

AGG Observations

Most of the examples FDA offers about impeding the agency's efforts to inspect are self-explanatory and are not controversial. FDA has the statutory authority to conduct inspections at reasonable times and in a reasonable manner. FDA also has the right to review certain types of records and data. However, a few observations are in order:

- FDA's inspectional authority is not unlimited. Yes, FDA has broad authority, but it is not unfettered. Companies must understand the statutorily-identified limitations, include such limitations in company procedures, and train personnel. A company must comply with FDA as required and, in a professional manner; however, the agency does not have carte blanche power during inspections.
- As noted, the guidance provides a number of examples of what FDA perceives to be unacceptable actions, unless there is a "reasonable explanation" offered by the company. However, because the phrase "reasonable explanation" is not defined, it appears FDA intends to rely on the investigator's subjective discretion to interpret a company's explanation and whether it is "reasonable." That subjective determination, even with additional review within the agency, will undoubtedly lead to challenges by the regulated industry in certain situations.
- FDA has maintained that it has the authority to take photographs. In the guidance, the agency reasserts its right but more formally. That said, the authority is not specifically described in the Federal Food, Drug, and Cosmetic Act, and many in industry continue to have company policies that discourage photographs. Any policy or company decision should include discussions with counsel.

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