Legal Backgrounder

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A Warning Letter on FDA's Expansive Interpretation of Its Facilities-Inspection Authority

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Dear FDA-Regulated Drug Establishment,

As an establishment that manufactures, distributes, or dispenses drugs, you were subject to an FDA inspection under § 704 of the Federal Food, Drug, and Cosmetic Act (FDCA). During this inspection, the FDA inspector asserted authority that is not explicit in the authorizing statute and that courts have not permitted. FDA expected that you, as a regulated drug establishment, would meet these demands immediately and without analysis of whether they were supported by law. Because you questioned how to comply with FDA's demands, and either did not comply in full or did not comply immediately, FDA is issuing this Warning Letter to you for delaying, denying, or limiting the inspection, which means that your drug products are hereby deemed adulterated under § 501(j) of the FDCA. As you know, you are prohibited from introducing adulterated drugs into interstate commerce under § 301 of the FDCA. Therefore, you are effectively ***shut down*** *based on the FDA inspector's subjective view of your conduct during this inspection.*

* * *

Although this hypothetical Warning Letter might seem ridiculous, it is not so far-fetched given the lack of clarity about the Food and Drug Administration's (FDA) inspection authority. While a "refusal" to permit inspection or access to certain records has long been a prohibited act under FDCA § 301, only recently have the terms "delay" and "limitation" become part of the FDA inspection jargon. In 2012, the Food and Drug Administration Safety and Innovation Act (FDASIA) added § 501(j) to the FDCA, which states that 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."[1] Congress required FDA to "issue guidance that defines the circumstances that would constitute delaying, denying, or limiting inspection, or refusing to permit entry or inspection, for purposes of section 501(j)."[2]

In October 2014, FDA issued a final version of that guidance document.[3] Rather than provide the clarity that Congress required, the Guidance reads like a list of FDA inspectors' pet peeves. Further, FDA misappropriated the purpose of the Guidance. Congress expected FDA to define the circumstances *within* FDA's inspection authority that would be a basis for a finding of adulteration, not to expand its inspection

[1] Food and Drug Administration Safety and Innovation Act, Pub. L. No. 112-144, § 707(a), 126 Stat. 993, 1068 (2012).
[2] *Id.* § 707(b).
[3] Circumstances that Constitute Delaying, Denying, Limiting, or Refusing a Drug Inspection (hereinafter "Guidance"), U.S. Dept. of Health and Human Serv., Food and Drug Admin. (Oct. 2014), *available at* http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM360484.pdf.

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authority and to demand compliance with unsupported requests during inspections. For example, FDA has long asserted that it is entitled to take photographs during inspections, but no court has confirmed it possesses such authority. Although regulated industry has serious concerns about FDA's use of photography during inspections, the Guidance addresses FDA's right to take pictures as if the issue is uncontroverted. The Guidance also fails to address the plain statutory language in § 704(a)(2) exempting from inspection records from pharmacies that operate in conformance with pharmacy laws and that do not engage in manufacturing. This issue is the source of repeated disputes during pharmacy inspections, but the Guidance does not provide much-needed clarity.

This LEGAL BACKGROUNDER analyzes the official Guidance and provides its own guidance to industry for how to prepare for FDA's assertion of questionable demands during inspections.

Legal Background

Section 704(a) of the FDCA is the authorizing provision that sets forth the scope of FDA's inspection authority. It allows FDA to enter a facility "at reasonable times," and to conduct such inspections "at reasonable times and within reasonable limits and in a reasonable manner."[4] FDA is permitted to inspect only the facilities, pertinent equipment, finished and unfinished materials, containers, labeling, and certain records (*e.g.*, files, papers, processes, controls, etc.) related to compliance.[5] The statute explicitly prohibits FDA from collecting financial, sales, personnel, or research data during inspections.[6]

"Guidance" on Dubious Inspection Practices

Taking Photographs During an Inspection. Even though Congress has never explicitly empowered FDA to take photographs, FDA has told its inspectors not to request permission from company management to do so, but rather to use a camera "as necessary just as [the inspectors] use other inspectional equipment."[7] FDA further advises its inspectors to tell a company's management that photographs "are an integral part of an inspection and present an accurate picture of firm conditions" and to warn the company that refusal can constitute a limiting of inspection, thus causing the product to be deemed adulterated.[8]

In the new Guidance, FDA ignores regulated entities' deep concern with photographs and dictates that companies have only a narrow basis for denying photography: if "the chemical properties of products manufactured at the facility are such that taking photographs would adversely affect product quality."[9] Absent this or a similar basis, the Guidance asserts that a company must permit inspectors to take photographs during an inspection or risk a claim of adulteration. Consequently, a regulated drug facility should be prepared for FDA inspectors to use cameras as part of their inspection and should seek advice from legal counsel concerning whether it can and should resist this activity.

Interviewing Employees. An FDA inspector may also attempt to question a company's subject-matter expert regarding operations of the facility. An employee's impromptu answers in response to FDA questions may become evidence for the government's use in a future enforcement action. Companies must clearly explain to their employees that, once provided, an impromptu answer is no less evidence than one

[4] FDCA § 704(a).
[5] *Id.*
[6] *Id.* ("No inspection . . . shall extend to 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 . . . .").
[7] FDA, Investigations Operations Manual § 5.3.4.1.
[8] *Id.*
[9] Guidance, *supra* note 3 at 7.

provided after thorough preparation and review of documents, and they should consider with advice of counsel whether and how to respond to such requests.

The FDCA does not empower FDA to require *any* employee (managerial or non-managerial) to answer questions during an inspection. While § 704 grants FDA the authority to inspect facilities, it does not compel employee testimony.

In the Guidance, however, FDA implies that it does possess such authority. For example, FDA claims it is reasonable to delay an unannounced inspection if "appropriate personnel are not immediately available to accurately answer the FDA investigator's questions."[10] It is unclear whether FDA would deem as "appropriate" only those employees the company has designated as subject-matter experts, or if FDA believes it has broad discretion to interrogate *anyone* at the facility.

It is understandable why many companies may permit FDA inspectors to question company employees upon request (or demand). Companies often believe that they have nothing to hide or that allowing access to employees will foster goodwill with FDA. Additionally, many companies may believe (whether by naïveté or persuasion) that FDA's statutory power to inspect includes the authority to question their employees.

Regardless of the reasons for allowing employee questioning, a company should be wary of the potential pitfalls from allowing FDA to question employees. It is essential that a company develops policies regarding employee questioning during an inspection. In the event that a decision is made not to comply with FDA interview requests, a company must be able to communicate clearly to FDA that its position is *not* a refusal or limitation, but simply compliance with well-established procedures governing the company's activities during FDA inspections.

Observing a Working Facility. FDA's Guidance states that "send[ing] staff home for the day and tell[ing] the FDA investigator that the facility is not producing any product" could constitute a denial of inspection, thus leading a facility's product to be deemed adulterated.[11] At the other end of the spectrum, FDA allows that a "potentially reasonable explanation[] that might result in the drugs not being deemed adulterated" would be that in connection with "an unannounced inspection[] the facility is closed due to scheduled maintenance."[12]

While it is not surprising that FDA would assert that a company cannot shut down manufacturing or other operations to evade an FDA inspection, FDA's Guidance provides little information as to when a lack of operations would result in a claim of adulteration. Industry is left wondering at what point FDA might assert that sending some employees home risks rendering a company's drugs adulterated.

Section 704 provides FDA with the authority to inspect facilities, but the statute does not entitle FDA to observe a facility in *active* operation. Specifically, the statute reads that FDA may inspect "such factory, warehouse, establishment, or vehicle and all pertinent equipment, finished and unfinished materials, containers, and labeling therein."[13] The language speaks to the *physical* facilities and not to the *functioning* of those facilities.

Again, a company should establish clear guidelines on which employees must remain on-site during an FDA inspection, and which are able to leave the premises without further scrutiny. A company should also delineate what operations must continue once begun, even if interrupted by an FDA inspection.

[10] *Id.* at 6.
[11] *Id.*
[12] *Id.*
[13] FDCA § 704(a)(1).

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Inspecting Records from Other Facilities. Section 704 requires FDA to provide "written notice" prior to an inspection, and states that "[a] separate notice shall be given for each such inspection." The Form 482 is the statutorily-required written notice to a facility that identifies the name and address of the premises subject to inspection. If FDA seeks to inspect additional sites beyond what is described on the Form 482, it must issue and present a new Form 482 to cover and authorize the subsequent inspection.

In discussing a company's requirement to produce records during an inspection, the Guidance implies FDA has authority to inspect records maintained at sites beyond the scope of the establishment named in the Form 482. Consider the following statement: "Although FDA recognizes that facilities require a reasonable amount of time to produce records requested, *especially if the records are maintained at a different site*, a delay in producing records to FDA without reasonable explanation may be considered delaying the inspection."[14] The Guidance offers no description of why FDA believes it has authority to inspect company records maintained off-site, or whether there is any limitation to such authority.

The language in § 704 reads that, during the course of a facility inspection, FDA is entitled to inspect "all things *therein* (including records, files, papers, processes, controls, and facilities)."[15] Thus, a plain reading of the statute suggests that FDA inspectors may only inspect records that are maintained at the facility under inspection. Section 704 does not grant FDA a general power to inspect all company-wide records by issuing a Form 482 to a single facility.

In this age of electronic records, centralized databases, and cloud storage, whether a record is maintained "therein" at a particular facility may be a complicated question. The manner of record storage should neither increase nor diminish FDA's inspection authority. Before responding to a request for records, a company should consider (with the assistance of counsel) whether the records requested fall within the scope of the inspection notice in the Form 482. Although FDA may have authority to ultimately inspect "other" records, it may be required to issue a new Form 482 identifying the different establishment charged with maintaining those records.

Conclusion

The ramifications of a "delay," "denial," "limitation," or "refusal" of inspection are substantial: an effective shutdown of operations because a company's drug product is *adulterated*. In enacting FDASIA § 501(j), Congress did not expand FDA's inspection authority contained in FDCA § 704, which remains the touchstone of the agency's inspection authority. The Guidance was expected to clarify areas of uncertainty in § 501(j), not to reiterate old questions or raise new ones for regulated industry regarding FDA's inspection power. Congress certainly did not mean for FDA to use the Guidance to expand its inspection authority.

Because of unresolved questions regarding FDA's inspection authority and aggressive inspection practices, a company must be aware of the agency's expectations during an inspection. Without forethought and putting internal policies in place specifically contemplating the issues discussed in this LEGAL BACKGROUNDER, a company runs the risk of being caught off-guard by an inspector's requests and possibly providing FDA with information beyond FDA's inspection authority. A company could be handing FDA evidence and information to which it would not otherwise be entitled, absent a subpoena, warrant, or other lawful process.

[14] Guidance, *supra* note 3 at 5 (emphasis added).
[15] FDCA § 704(a)(1) (emphasis added).

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