



**Prevention is Key:
Steps to Prepare for and
Respond to a FDA
Inspection or
Enforcement Action**

#NCPA2016

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NATIONAL COMMUNITY
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Disclosure

Jeffrey S. Baird, Esq., is Chairman of the Health Care Group at Brown & Fortunato, P.C. The conflict of interest was resolved by peer review of the slide content.

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Learning Objectives

- Discuss the legal arguments for and against FDA jurisdiction over pharmacies.
- Create a preparation protocol for an FDA inspection or enforcement action.
- Outline steps your pharmacy can take in responding to an FDA inspection or enforcement action.

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Introduction

- Pharmacies have been an integral component of our nation's health care delivery system since the foundation of our country.
- Until the 1930s, pharmacies were subject to very little government oversight.

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Introduction

- Beginning in the first half of the 20th century, particularly with the advent of the Food and Drug Administration and the Drug Enforcement Administration, the federal government began to take an increasing role in regulating pharmacies.

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Introduction

- The same can be said for the states. Beginning in the first half of the 20th century, state boards of pharmacy became more active in regulating pharmacies operating in their states.

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Introduction

- Nevertheless, compared to other health care providers (hospitals, physicians, labs, etc.), regulatory requirements imposed on pharmacies were not particularly stringent.
- This has changed and there are several reasons for the change.

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Introduction

- With few exceptions pharmacies did not bill Medicare. As a result, there was not a great deal of federal governmental scrutiny of pharmacies. But then there was a “sea change.”
- In the first decade of the 21st century, Medicare began paying for prescription drugs for Medicare beneficiaries under Part D. As a result, Medicare now has serious “skin in the game.”

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Introduction

- Because Medicare is paying a great deal of money for prescription drugs, Medicare is motivated to scrutinize pharmacy operations to insure that Medicare funds are being wisely spent.
- The same can be said of TRICARE. For the past several years, a number of pharmacies submitted large numbers of claims to TRICARE for compounded drugs ... particularly pain and scar creams.

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Introduction

- TRICARE paid these claims until it concluded that the pharmacies were “gaming the system,” at which time TRICARE ceased paying for compounded drugs and launched investigations of compounding pharmacies.
- Because pharmacies are billing Medicare under Part D, and are billing TRICARE, the pharmacies must comply with an array of federal anti-fraud laws such as the Medicare anti-kickback statute and the False Claims Act.

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Introduction

- The primary users of maintenance prescription drugs are the elderly.
- Until recently, the elderly primarily consisted of the 23 million of the “Greatest Generation.”
- The Greatest Generation is being replaced by 78 million “Baby Boomers” who are retiring at the rate of 10,000 per day.

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Introduction

- As a result, the demand for health care services, including prescription drugs, is increasing exponentially.
- This is resulting in large outlays by Medicare and other government programs ... resulting in motivation on the government’s part to scrutinize pharmacy operations.

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Introduction

- As Baby Boomers age, the demand for health care is increasing exponentially.
- However, government programs do not have an infinite amount of money to pay for health care.
- This is the classic “irresistible force meeting the immovable object.”

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Introduction

- The interplay between increasing demand and limited money has resulted in lower reimbursement for pharmacies.....resulting in narrower profit margins.
- Unfortunately, human nature being what it is, there are a number of pharmacies trying to “game the system” to make up for the narrower profit margins.

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Introduction

- Examples of “gaming the system” include:
 - Pharmacy pays 1099 independent contractor marketing reps to generate patients for the pharmacy.
 - Pharmacy directly or indirectly provides “items of value” to physicians and other referral sources.
 - Pharmacy offers gifts and other inducements to prospective patients.

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Introduction

- Cont'd
 - Pharmacy ships prescription drugs into states in which the pharmacy does not have an out-of-state pharmacy license.
 - Pharmacy routinely waives all or a portion of the patient's co-payment.
 - Pharmacy enters into a “sham” clinical study program whose purpose is to funnel remuneration to prescribing physicians.
 - Pharmacy compounds drugs that are commercially available.
 - Pharmacy engages in a large-scale compounding operation that resembles manufacturing.

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Introduction

- These types of questionable actions by pharmacies have resulted in increased scrutiny by governmental agencies.
- The following slides discuss FDA inspections. In particular, the slides discuss how the pharmacy can prepare for, and respond to, an FDA inspection.

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FDA Inspection: Overview

- Section 704(a)(1) of the Federal Food, Drug, and Cosmetic Act. 21 U.S.C. § 374(a)(1). It allows FDA investigators to enter, at reasonable times, facilities in which drugs are manufactured, processed, packed, or held for introduction into interstate commerce. In addition, Section 704(a)(4) of the Federal Food, Drug, and Cosmetic Act allows the 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 other information that may be inspected under Section 704(a).

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FDA Inspection: Overview

- There are three basic categories of inspections:
 - A **COMPREHENSIVE INSPECTION** is requested by FDA headquarters or the district office and can cover everything in the pharmacy subject to FDA jurisdiction. These inspections can take less than a day, or they may last for weeks.
 - An **ABBREVIATED INSPECTION** is an inspection that covers only critical factors that are identified in the Inspectional Guidelines, the FDA Investigations Operations Manual (IOM), or under an inspectional program from FDA headquarters.
 - A **DIRECTED INSPECTION** is triggered by an identifiable event, such as a recall, consumer complaint follow-up, competitor complaint, or other specific incident.

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FDA Inspection: Overview

- Regardless of the type of inspection, the key issue will be whether the pharmacy is a manufacturer. If the inspector believes that the pharmacy is a manufacturer, he or she will issue an FDA-483 Inspectional Observations.
- The final decision as to whether a pharmacy is a manufacturer will be made by FDA headquarters in Silver Spring, Maryland.

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FDA Inspection: Overview

- Key personnel should be familiar with their roles in dealing with the investigator. (Although pharmacy inspections ordinarily involve only one FDA investigator, the agency can send two or more investigators.) Once the inspection begins, it is crucial that the key personnel in all operations promptly be made aware of the presence of the FDA. If a corporate Inspection Leader is not available to respond to the FDA, other personnel need to understand the pharmacy's policies when answering the investigator's inquiries.

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FDA Inspection: Overview

- FDA inspections are usually unannounced. Thus, the pharmacy must be prepared for an inspection at any time.
- Contacts with FDA investigators require the utmost professionalism. Investigators have a job to perform. The FDA's Investigations Operations Manual says that investigations "must always be conducted with tact, honesty, diplomacy, and persuasiveness." § 5.2.5.4.

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FDA Inspection: Overview

- Do not create an adversarial environment; it is counterproductive. On the other hand, the pharmacy must recognize that the investigator is not there to befriend it. No matter what the investigator says, the investigator is not there for the pharmacy's benefit.
- The investigator should be courteously received during the course of his or her visits. Usually, this attitude will achieve the best results for the pharmacy and establish a better long-term relationship with the FDA. Conversely, a series of confrontations with the investigator can cause an otherwise manageable situation to deteriorate rapidly.

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FDA Inspection: Overview

- The degree of corporate cooperation will be reflected in the investigator's Establishment Inspectional Report ("EIR"). The EIR is an internal FDA document that comprehensively describes the inspection. The EIR describes all aspects of the investigation, e.g., the history of the pharmacy, pharmacy management, inspectional findings, the lay-out of the facility, discussions with management about problems, etc. The pharmacy's attitude will be reflected in the EIR, which will then go into the FDA's permanent file on the pharmacy. It is often helpful to obtain a copy of the EIR through a Freedom of Information Act request once the inspection has been concluded.

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FDA Inspection: Overview

- An Inspection Leader must be assigned to deal with the FDA. This designated individual may also be appointed to handle the telephone communications. This leader should be aware of all aspects of the pharmacy's policies, operations, and record-keeping systems.
- Alternatively, an Inspection Group can be set up. This group would then assign a Leader who would be responsible for the group's actions. The group would be made up of persons familiar with the pharmacy's policies for dealing with the FDA and with the pharmacy's operations.

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FDA Inspection: Overview

- The Leader and/or the group should accompany the investigator throughout the inspection.
- The FDA may follow-up the inspection with a telephone call. All telephone calls from the FDA should be handled by the pharmacy's Inspection Leader.

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FDA Inspection: Overview

- The investigator should be made aware at the outset that there is a pharmacy policy for dealing with the FDA. This will help when questions arise on how to answer the inquiries made by the investigator. An FDA investigator will more readily accept a denial based on established policy than a refusal based on an “instant policy” created on the spot. In responding to issues such as the taking of photographs, access to corporate records, and signing affidavits, as well as other problem areas, politely explain that the investigator’s request cannot be granted because of an existing pharmacy policy.

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Inspection Authority

- Section 501(j) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 351(j), deems a drug to be 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.”

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Inspection Authority

- If the pharmacy refuses inspection, the FDA's recourse would be to obtain a search warrant allowing it entry onto the premises. There is no legal basis for completely refusing an inspection, except if the FDA wishes to inspect at an unreasonable time. Refusal can lead to an FDA enforcement action. It also injures the relationship with the agency. Thus, refusal is almost never a viable option. However, the inspection must be at a reasonable time.

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Inspection Authority

- Sometimes a pharmacy will allow the FDA to inspect the facility, but refuse to show certain records. The investigator may say that this "partial refusal" violates § 331(f). However, although the investigator may cite § 331(f), this provision applies only if the FDA does actually have inspectional authority over those documents. In the event of a partial refusal, investigators generally will telephone their supervisor for instructions.

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Inspection Authority

- A pharmacy is not subject to the FDA's full inspectional powers. However, if the pharmacy "crosses the line" to being a manufacturer, then it will be subject to full inspection. Relying on its status as a pharmacy, the pharmacy can elect to tell the investigator that he has no right to see "manufacturing" records and related documents.

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Inspection Authority

- The investigator will want to examine "manufacturing" records to see if the pharmacy is complying with current good manufacturing practices (GMPs) for drugs. It is not. The issue is not GMP compliance; it is whether the pharmacy is a "pharmacy" or a "manufacturer." The pharmacy should politely try to get the investigator to focus on this point, and not on GMP compliance.
- Be sure that prior to any inspection the investigator issues a "Notice of Inspection" Form FDA-482 and that his credentials are up to date.

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Inspection Authority

- Section 704(a)(4) of the Federal Food, Drug, and Cosmetic Act also allows the FDA to request, in advance of or in lieu of an inspection, any records or other information that may be inspected under Section 704(a). 21 U.S.C. § 374(a)(4). The failure to produce the records requested by the FDA pursuant to Section 704(a)(4) in a timely manner may cause drugs to be adulterated. Consequently, refusing to respond to such a request is usually not a viable option. However, the request must be within a reasonable timeframe, within reasonable limits, and in a reasonable manner.

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Proprietary Information

- Special attention should be paid to records that contain proprietary information. These documents should be marked "**CONFIDENTIAL - TRADE SECRET,**" and this fact should specifically be called to the attention of the investigator. Make sure that the investigator notes that the material is considered trade secret information. This notation minimizes the risk that the information will be disclosed to third parties under the Freedom of Information Act ("FOIA"). Be aware, though, that too many claims of confidentiality may cause the FDA to view all claims of confidentiality skeptically.

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Proprietary Information

- Generally, FDA personnel are barred from disclosing any trade secret information to anyone outside the agency. 21 U.S.C. § 331(j); 18 U.S.C. § 1905. However, the FDA may release these documents to Congress. Congress is not bound by the same obligations to preserve confidentiality.

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Proprietary Information

- All documents in the FDA's files are potentially subject to release under FOIA. Probably the best solution is to stamp "Confidential - Trade Secret" on each copy of any proprietary documents provided to the investigator. This will alert the FDA employee responsible for handling the FOIA request to the confidentiality claim.
- The pharmacy may have internal audit files on hand. These files would contain the findings of inside auditors or outside consultants. Audits do not have to be shown to the FDA. The FDA has said that it will not typically request these audits.

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Proprietary Information

- The pharmacy will have patient records. The pharmacy can reasonably ask that the investigator not seek to copy records that contain patient identifiers. Alternatively, the pharmacy may tell the investigator that the pharmacy wishes to delete patient identities from copied documents.

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Information to Which the FDA is Not Entitled

- Because financial data may bear upon the pharmacy/manufacturer dichotomy, it is possible that the investigator will request sales information. The FDA does not have authority to obtain financial information. The pharmacy should decide in advance whether it wants to give this information. The FDA is also not authorized to inspect sales data, pricing data, research data, and personnel data (other than technical qualifications). The pharmacy does not have to release marketing plans or similar information.

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Information to Which the FDA is Not Entitled

- It is the pharmacy's responsibility to understand these limits. The FDA investigator is not obliged to advise the pharmacy that a request is outside the scope of the FDA's authority. If the FDA investigator asks for the documents, and the pharmacy voluntarily provides them, the documents can be used against the pharmacy. The FDA's investigators generally know these limits, and will respect a denial. They ask for the information because they know that many pharmacies will provide these documents even though they do not need to do so.

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Copying of Documents

- The FDA may request records in advance of or in lieu of an inspection under Section 704(a)(4) of the Federal Food, Drug, and Cosmetic Act. Upon receipt of such a request, the pharmacy is required to provide the requested records and information in a timely manner, in either electronic or physical form, at the expense of the pharmacy. Absent a request for records under Section 704(a)(4), however, the pharmacy is not required to supply the FDA investigator with a photocopy of its records. So what should you do if the FDA inspector asks to copy records?

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Copying of Documents

- The longer the investigator is present, the more likely a problem could arise. It is sensible (and customary) to make the copies for the investigator. Always make a duplicate set of copies for the pharmacy's own records. These copies should go in the pharmacy's "Inspections File." If the copying is extensive, the pharmacy can charge the agency for the service, although this is not normally done. The investigator should be asked to initial and date the back of the original record to identify the record that the copy came from.

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Copying of Documents

- Do not let the investigator have free access to the photocopying machine. Someone should be present with the investigator at all times. Have someone do the copying for the investigator. Nor should the pharmacy let the investigator have unrestricted access to the files -- provide only those documents that are specifically requested.
- Copies of proprietary records, if supplied to the agency, should be stamped "Confidential - Trade Secret." Do not let copies of these records out of the pharmacy without imprinting that statement.

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Samples

- The FDA may collect samples of product, e.g., compounded drug and the accompanying label.
- Use the following procedures:
 - Always take a duplicate sample from the same batch for your review and testing.
 - Ask the agency what tests are going to be performed so that duplicate tests can be done by the pharmacy's laboratory. For example, the FDA may want to conduct sterility tests.
 - The pharmacy can charge the agency for samples, but this is not usually done for samples of nominal value. If the samples are expensive, the pharmacy may legitimately request reimbursement.

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Samples

- The pharmacy should get a Receipt for Sampling Form FDA-484 from the investigator. The investigator should provide the pharmacy with the original FDA-484. The investigator may ask the pharmacy to sign the FDA-484. There is no harm in doing so, but there is no benefit either. The easiest policy to implement is an absolute prohibition against employees signing any FDA document.
- In some circumstances, the pharmacy may want to consider refusing sampling by the agency. Ordinarily, though, the FDA can obtain a sample through some other means. Moreover, declining to allow FDA to collect samples may cause drugs to be deemed adulterated. Thus, this type of refusal is usually futile and probably counterproductive.

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Photographs - Samples

- “Pictures are worth a thousand words.” Or, as the FDA Investigations Operations Manual says, “photographs are one of the most effective and useful forms of evidence.” § 5.3.4. This is surely true when used as direct evidence in litigation.
- The best corporate policy is “**NO CAMERAS ARE ALLOWED IN THE FACILITY.**” This is to protect trade secrets, patient privacy, and compounding procedures. A sign stating this policy should be posted at the reception desk. By giving this type of notice, the pharmacy may prevent a direct confrontation with the FDA investigator on the subject of photography.

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Photographs - Samples

- The FDA's draft guidance on circumstances that constitute delaying, denying, limiting, or refusing an inspection states that “[p]hotographs are an integral part of an FDA inspection because they present an accurate picture of facility conditions. Not allowing photography by an FDA inspector may be considered a limitation if such photographs are determined by the investigator(s) to be necessary to effectively conduct that particular inspection.” The pharmacy should also be aware that the investigator may say that the FDA has the right to photograph as a result of a Supreme Court decision.

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Photographs - Samples

- Citing that case, a June 13, 1986, FDA field memorandum says that “photographs are an integral part of an inspection and should be taken.” The case relied on by the FDA involved the Environmental Protection Agency’s right to photograph a facility from a plane. No trade secret information was photographed. Regardless of what the investigator says, the FDA has no clear statutory or legal authority to support taking pictures.

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Photographs - Samples

- More often than not, an FDA investigator will not insist upon photographs if it is demonstrably forbidden by pharmacy policy. Occasionally, however, the investigator will feel very strongly about this issue. This is most likely to occur when the investigator has observed particularly deplorable conditions, e.g., rodent infestation in food warehouses. The FDA has gone to court from time to time to obtain a warrant authorizing the use of a camera.

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Signing Official Documents

- An official of the pharmacy may be asked to supply copies of shipping records or invoices, and then to sign documents identifying the source, verifying shipment, or confirming other information on the status of any sample the FDA collects. Or the pharmacy may be asked to confirm in writing its compounding and dispensing practices. This is usually in a form of an “affidavit” prepared by the FDA. The FDA has no authority to compel the pharmacy to sign anything.

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Signing Official Documents

- The policy for signing such forms or statements should be established in advance. Signing the document does not benefit the pharmacy in any way. The better approach is to have pharmacy officials refuse to sign or to even give an oral “OK” that the statement is correct. (The FDA investigator would note a verbal affirmation and use it against the pharmacy).

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Signing Official Documents

- One trick the FDA investigator might use is to prepare the affidavit in the pharmacy's name and then make a mistake and ask the pharmacy to initial the error. By doing this, and not correcting elsewhere, the pharmacy could be impliedly indicating that it had read the affidavit and did not disagree with it. Similarly, if the pharmacy does read the affidavit and feels it is incorrect in a specific statement, it may be tempted to point out the error. The FDA might then argue that identifying only a single error implies that the pharmacy agrees with all other statements.

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Signing Official Documents

- Another ploy would be for the FDA investigator to state on the affidavit that "the pharmacy refused to sign the affidavit" and ask the pharmacy to sign that statement. The pharmacy should not sign or initial the affidavit if it has already decided not to sign the affidavit or other official forms.
- Signing or orally acknowledging a statement could be used against the pharmacy in a future enforcement action. Declining to sign would not protect the pharmacy from further actions but does make the agency's job harder in documenting its case. The most prudent policy is not to sign any document prepared by the FDA.

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Establish an Inspections File

- After each inspection, the pharmacy should create a separate file. This file will include the notes taken during the inspection by pharmacy employees, the forms filled out regarding the inspection, duplicates of the records copied by the investigator, the FDA-482 Notice of Inspection, the FDA-483 Notice of Observations, the FDA-484 Receipt of Samples, the pharmacy's analytical results for samples tested, and any subsequent correspondence with the agency.
- Maintaining all information in a single file will make it easier to reconstruct the circumstances of the inspection years later, if necessary. Never show this file to the FDA, or to anyone outside the pharmacy who is not bound by confidentiality.

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Gifts

- Without question, gifts should never be offered to any investigator. It is a federal offense to give a gift to a federal agent.

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Meals

- The pharmacy should not offer to take the investigator to lunch. FDA employees are prohibited from accepting meals from regulated industry. It is not inappropriate to offer coffee, tea or a soft drink if that is the customary practice for all visitors.
- If the pharmacy wants to have lunch with the investigator, let him pick up his own bill. It is much better, though, to recommend a restaurant where the investigator can eat without being accompanied by a pharmacy employee.

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FDA-483 (List of Observations) Response

- At the inspection's end, the investigator will have an exit interview with management to detail the findings of the inspection and to obtain the pharmacy's comments.
- If no FDA-483 is issued, the investigator may still have some recommendations for how to improve the pharmacy's operations. Sometimes, an investigator will suggest some way in which a pharmacy can strengthen its claim to be a pharmacy, not a manufacturer. Or the investigator may make a suggestion about shelf-life testing.

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FDA-483 (List of Observations) Response

- In such a case, listen and take all suggestions under review but do not promise implementation. No further follow-up is necessary for this type of exit interview.
- If an FDA-483 is issued, the investigator is going to request a direct and immediate response. It would be advisable to review each point for clarification with the investigator, but make no comments regarding follow-up action unless the pharmacy is certain that a specific action can and will be taken. Explain that the list will be reviewed by management, and a written response soon will be mailed to the district office.

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FDA-483 (List of Observations) Response

- One section of the establishment inspection report (“EIR”) specifically addresses the exit interview. Statements made during the exit interview will be reported in detail in the EIR. Do not reject observations out-of-hand, become defensive, or be unwilling to listen; on the other hand, make commitments sparingly. Any commitments will be recorded. The safest response is of the “We have no comment on that at this time” variety.

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FDA-483 (List of Observations) Response

- In preparing a written response to the FDA-483, make sure it is timely and accurate. If there are significant or numerous observations, the pharmacy should consult with regulatory counsel before responding. The FDA's current policy is to try to issue Warning Letters within a few weeks of the completion of the inspection. A Warning Letter would state that the pharmacy has violated the law in some respect; this letter is made publicly available. The response should be received by the FDA within ten days or so. If necessary, a supplemental response can be submitted later.

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FDA-483 (List of Observations) Response

- Each observation in the FDA-483 will be separately numbered. The response letter should address each point individually. Give a detailed reason for any disagreement with the findings. When responding to a valid point, concisely explain how the pharmacy will modify its conduct or what changes will be made. Do not admit that there was an error or flaw; rather, just describe the new procedures.

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FDA-483 (List of Observations) Response

- Give a target date for corrective actions to be implemented. This date should be realistic.
- All responses should be made in a positive tone and in a spirit of cooperation. The response to the FDA-483 is part of the FDA's permanent record and is made available to third parties through the Freedom of Information Act. If trade secret information is enclosed, identify the portions that are confidential and ask the FDA not to release those sections of the letter.

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Letter Response to FDA Form 483

- The following slides contain excerpts from a letter, by a pharmacy to the FDA, that responds to an FDA Form 483.

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Letter Response to FDA Form 483

- The Food and Drug Administration (“FDA”) conducted an inspection of _____ (the “Pharmacy”), a pharmacy located at _____, between _____ and _____. Upon the conclusion of its inspection, the FDA provided the Pharmacy with an FDA Form 483. Please accept this letter as the Pharmacy’s response to the observations raised in the FDA Form 483. We respectfully request that this response, excluding the attachments, be posted on the FDA’s website with the Form 483 and be included every time the FDA provides a copy of the Pharmacy’s FDA Form 483 to any individual or entity outside the FDA.

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Letter Response to FDA Form 483

- To the extent the observations cited in the Form 483 are based on the current Good Manufacturing Practices (“cGMPs”) for finished pharmaceuticals, such observations are inapplicable to the operations of the Pharmacy. The cGMPs are requirements imposed upon either drug manufacturers or registered outsourcing facilities. The Pharmacy does not engage in drug manufacturing nor has it registered as an outsourcing facility under 21 U.S.C. § 353b. The Pharmacy remains a traditional pharmacy licensed by the _____ Board of Pharmacy as a retail pharmacy and is subject to its jurisdiction.

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Letter Response to FDA Form 483

- The FDA's cGMPs for finished pharmaceuticals are not applicable to the Pharmacy or any compounded medications it prepares. 21 U.S.C. § 353a specifically exempts a compounding pharmacy from the cGMP requirements imposed on a drug manufacturer by 21 U.S.C. § 351(a)(2)(B).

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Letter Response to FDA Form 483

- The Pharmacy operates in compliance with the requirements of 21 U.S.C. § 353a, applicable state laws and regulations governing pharmacy compounding, and with the United States Pharmacopoeia ("USP") chapters <795> and <797>. The Pharmacy compounds primarily patient-specific prescriptions in compliance with the laws of _____ and any other state in which it conducts business. The Pharmacy also prepares medications for administration in the offices of licensed local prescribing practitioners upon the receipt of their orders, as permitted by _____ state law.

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Letter Response to FDA Form 483

- Specifically, _____ Admin. Code tit. _____ states that “[t]he pharmacy may compound drug products to be used by practitioners in their office for administration to patients.” Therefore, the Pharmacy is exempt from complying with cGMPs applicable to drug manufacturers under 21 U.S.C. § 351(a)(2)(B).

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Letter Response to FDA Form 483

- However, to the extent that the FDA contends that the Pharmacy is not protected by Section 353a for medication prepared and dispensed to practitioners for administration, we reiterate that such practice is expressly authorized by the _____ legislature and the _____ Board of Pharmacy. We further believe that Congress did not intend to allow the FDA to prohibit pharmacy compounding for office use in states where it is expressly allowed and regulated. In a letter to the FDA dated June 27, 2014, members of the U.S. Congress clarified its intent as follows:

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Letter Response to FDA Form 483

- Pharmacies that produce small amounts of compounded products in advance of receiving a patient-specific prescription and practice within States where office use is authorized and regulated by State Boards of Pharmacy should not be the focus of FDA oversight. Expecting these small pharmacies that practice in accordance with State law to register as outsourcing facilities solely because products are intended for office use is unreasonable. As FDA prioritizes its resources in a way that best protects public health, we believe the focus should be on manufacturers, not small pharmacies providing safely-compounded products for the physicians and hospitals in their communities.

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Letter Response to FDA Form 483

- More recently, in the House Agriculture Appropriations Committee Report dated July 14, 2015, the U.S. Congress again reiterated its belief that the FDA has, by attempting to regulate office-use compounding, overstepped its statutory authority. Specifically, Congress stated that office-use compounding is authorized in “the vast majority of states and was intended to be allowed” under 21 U.S.C. § 353a. Furthermore, Congress directed the FDA to issue guidance allowing pharmacies to engage in office-use compounding before the receipt of a patient-specific prescription in a manner consistent with the provisions of Section 353a.

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Letter Response to FDA Form 483

- For these reasons, the Pharmacy challenges the FDA's observations on the grounds that the cGMPs are not applicable to its compounding pharmacy operations. The Pharmacy complies with all applicable state and federal laws. In particular, the Pharmacy adheres to the USP chapter <797> guidelines for compounding sterile drug products. Our pharmacy is dedicated to ensuring that our sterile and non-sterile drugs are prepared in a safe and effective manner.
- Our responses to the observations raised in the Form 483 are as follows:
 - The letter responds to each observation set out in FDA Form 483.

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Letter Response to FDA Form 483

- With this response, the Pharmacy has sought to address all of the FDA's observations and concerns. While cGMP requirements are not applicable to the pharmacy's operations, we have accepted the FDA's observations as suggestions for improvement and will implement additional best practices to the extent feasible and compatible with our obligations under state law and the USP guidelines. If the FDA requires additional information or communication from the Pharmacy, please contact me at _____.

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FDA Warning Letter to Pharmacy

- The following slides are excerpts from a warning letter to a pharmacy.

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FDA Warning Letter to Pharmacy

- From _____ to _____, U.S. Food and Drug Administration (FDA) investigators conducted an inspection of your facility, _____, located at _____.

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FDA Warning Letter to Pharmacy

- During this inspection, the FDA investigators observed serious deficiencies in your practices for producing sterile drug products, which put patients at risk. For example, our investigators noted that your firm did not establish an adequate contact time for your sporicidal agent used to disinfect your aseptic processing areas. Furthermore, your firm failed to demonstrate through appropriate studies that your hoods are able to provide adequate protection of the ISO 5 areas in which sterile products are processed. Therefore, your products may be produced in an environment that poses a significant contamination risk.

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FDA Warning Letter to Pharmacy

- FDA issued a Form FDA 483 to your firm on _____. FDA acknowledges your firm's responses to the Form FDA 483, dated _____.

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FDA Warning Letter to Pharmacy

- The FDA investigators observed that your drug products intended or expected to be sterile were prepared, packed, or held under insanitary conditions, whereby they may have become contaminated with filth or rendered injurious to health, causing your drug products to be adulterated under section 501(a)(2)(A) of the FDCA [21 U.S.C. §351(a)(2)(A)]. For example, the FDA investigators noted that your firm did not establish an adequate contact time for your sporicidal agent used to disinfect your aseptic processing areas. Furthermore, your firm failed to demonstrate through appropriate studies that your hoods are able to provide adequate protection of the ISO 5 areas in which sterile products are processed. Therefore, your products may be produced in an environment that poses a significant contamination risk.

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FDA Warning Letter to Pharmacy

- We acknowledge your responses to the Form FDA 483 inspectional observations, dated _____. Although several of your proposed corrective actions appear adequate, others are deficient. For example, in your response to our observation regarding _____, your firm amended its cleaning and disinfection policy to include _____. However, the manufacturer recommends that _____ for use as a sporicide, and you did not provide documentation to justify this reduced dwell time.

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FDA Warning Letter to Pharmacy

- FDA strongly recommends that your management immediately undertake a comprehensive assessment of your operations, including facility design, procedures, personnel, processes, materials, and systems. In particular, this review should assess your aseptic processing operations. A third party consultant with relevant sterile drug manufacturing expertise could be useful in conducting this comprehensive evaluation.

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FDA Warning Letter to Pharmacy

- The violations cited in this letter are not intended to be an all-inclusive statement of violations at your facility. You are responsible for investigating and determining the causes of the violations identified above and for preventing their recurrence or the occurrence of other violations. It is your responsibility to ensure that your firm complies with all requirements of federal law, including FDA regulations.
- You should take prompt action to correct the violations cited in this letter. Failure to promptly correct these violations may result in legal action without further notice, including, without limitation, seizure and injunction.

New Orleans

FDA Warning Letter to Pharmacy

- Within fifteen working days of receipt of this letter, please notify this office in writing of the specific steps that you have taken to correct the violations. Please include an explanation of each step being taken to prevent the recurrence in violation of the FDCA, include your reasoning and any supporting information for our consideration.

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Response to FDA Warning Letter

- The following slides are excerpts from a letter by a pharmacy to the FDA that responds to a warning letter.

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Response to FDA Warning Letter

- Our office recently received the above-referenced Warning Letter from the Food and Drug Administration (“FDA”). The Warning Letter follows from a review of _____’s (“Pharmacy”) initial and updated responses to the inspectional observations identified in a _____, FDA Form 483. The Form 483 was issued as a result of an inspection by the FDA of Pharmacy in _____.

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Response to FDA Warning Letter

- This letters serves as Pharmacy’s formal response to the Warning Letter, and we ask that the FDA publish this letter, excluding any exhibits, on the FDA’s website and disclose this information any time the FDA provides a copy of Pharmacy’s Form 483 or the Warning Letter to a person or entity outside of the agency.

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Response to FDA Warning Letter

- As we stated in our initial response letter dated _____, the deficiencies cited by the FDA Form 483 and the Warning Letter are inappropriately based upon the current Good Manufacturing Practices (“cGMPs”) for finished pharmaceuticals established in 21 C.F.R. §§ 210 and 211 and further explained in the FDA’s *Industry Guidance on cGMPs for Sterile Drug Products Produced by Aseptic Processing*.

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Response to FDA Warning Letter

- Please note that the latter is non-binding guidance only. In addition, as Pharmacy employs a state-licensed pharmacist to compound drug products primarily for identified individual patients pursuant to a valid prescription order, Pharmacy is exempt under 21 U.S.C. § 353a(a) from complying with 21 U.S.C. § 351(a)(2)(B), which requires that a drug product and any facilities used in its manufacturing conform with cGMPs.

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Response to FDA Warning Letter

- In addition, while Pharmacy compounds limited quantities of _____ medications for office use by _____ practitioners, such practice is expressly permitted by the _____ Board of Pharmacy and, therefore, should be excluded from FDA oversight in accordance with Congress's June 27, 2014, letter to the FDA regarding the ability of the agency to regulate community-based pharmacies. As a 503A entity that neither engages in drug manufacturing nor is registered as a 503B outsourcing facility, the cGMPs are inapplicable to the operations of Pharmacy.

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Response to FDA Warning Letter

- In any event, the outstanding issues identified in the Warning Letter have also been addressed by Pharmacy's current policies and procedures to the extent that such observations constitute a "best practice" that, if adopted, would benefit the safety of Pharmacy's patients. Specifically, the Warning Letter identified three separate areas of concern. These concerns, along with Pharmacy's corresponding responses and actions, are set forth below.
 - The letter then addresses the areas of concern set out in the FDA's warning letter.

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Response to FDA Warning Letter

- Through this response, Pharmacy seeks to address all of the FDA's remaining observations and concerns. If the FDA requires additional information or communication from Pharmacy, it is welcome to contact me at _____.



100 Daingerfield Road
Alexandria, VA 22314-2885
703.683.8200 | Fax 703.683.3619
www.ncpanet.org

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