

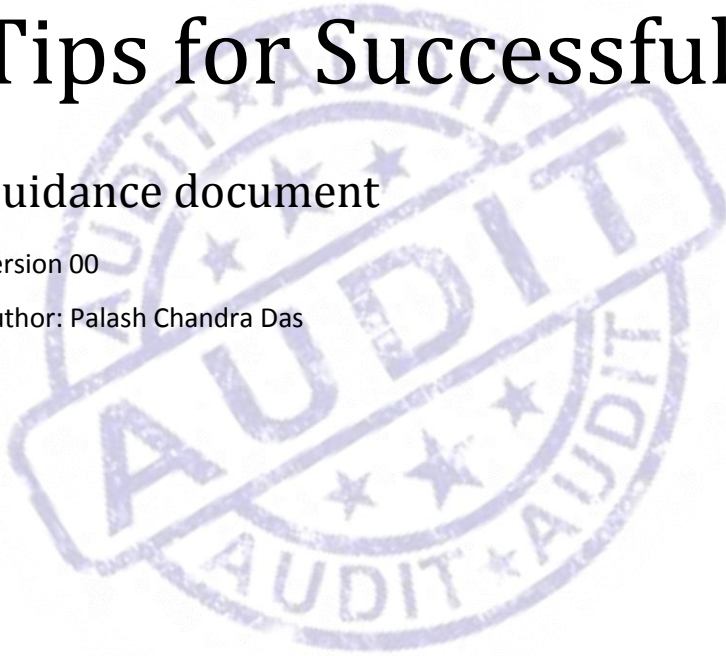


# Tips for Successful FDA Audit

Guidance document

Version 00

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## From The Author's Desk

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*Dear Readers,*

*Through PRES we are trying to connect with the Global Pharma community. Where we discussed, share and explore lots of pharmaceutical hot topics. Being a Pharma professional it is very difficult to get time for own to do something different other than routine responsibilities. Hope you all paraprofessionals are agreed with my views.*

*That's you, the readers and followers of my blog, who always encouraged me a lot to do something different than my routine schedule. All the information are easily available web media, I am just trying too collate all those information in a single article.*

*I have collated the information's broadly from the Pharmacompliancemonitor, FDA and other regulatory website for this article.*

*Once again I would like to thanks my readers, followers and seniors, who has encourage me a lot.*

### ***PRES Mission***

*To develop scientifically sound, practical, technical information and resources to advance science and regulation for the pharmaceutical industry*

### ***PRES Vision***

*To be the foremost global provider of science, technology, and regulatory information and education for the pharmaceutical community*

## Author



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*Mr. Palash Chandra Das is recognized as an expert in the field of aseptic manufacturing of parenteral products, and is a frequent presenter at several web conferences and technical training for Sterile Drug Manufacturing.*

*He earned his master's for Pharmaceutical chemistry from the University of West Bengal University of technology in India.*

*Since 2011 Palash has associated with installation, qualification and operation several production-lines in standard Clean room Technology as well as in Isolator Technology at major regulatory facility across India.*

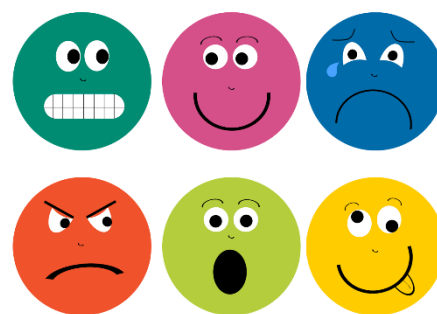
**A**nnouncements of Inspection are always a nightmare for pharmaceutical industry. We did not feel that it was good news at all. Thought like 483, warning letter and recall are always come to our mind.

In this article we will discuss elaborately, how to overcome from this kind of circumstances. Fear, Anxiety, Panic, stress, pressure, tension and worry all are represent our mental state of mind. Normally two types of feelings we have, one is positive feeling one is negative feelings. Positive feelings always make us happy and it visible through our facial expression. Negative feelings always come up with stress and pressure.

The quality of your life is largely determined by the quality of the mental states you live in day to day – states like love, anger, happiness, fear and excitement. There are two main ways to control your state of mind. Either by controlling the way you use your physical body, or by controlling your focus of attention and the way you interpret it. What happens in your life does not determine how you feel. How you feel is only the result of how you are using your own mind and body at any moment.



No matter what happens in your life, you are in control of your own state of mind. Make sure to use that ability to put yourself in a state that is appropriate for what you want to achieve. In most cases, would it not be nice to be in a highly positive mood most of the time? People in our society often turn to external means such as food, alcohol, cigarettes or



drugs to elevate their mood, but with the techniques you are about to learn you will not have to depend on anything outside of yourself to change the way you feel.

For example, a person who is depressed will look down, talk slowly, have shallow breath, slackened facial muscles and will be physically hunched over. Conversely, a happy and positive person will smile, talk faster, raise their shoulders, lift their head and breathe deeply. We also become happy when we take action towards something that is important to us, while on the other hand depression comes from inertia. You cannot be sad and busy at the same time.

Are you surprised that in spite of discussing on technical aspect, we are discussing about behavioral aspects. Because the way we communicate to the auditor that matters a lot.

Effective communication is about more than just exchanging information. It's about understanding the emotion and intentions behind the information. As well as being able to clearly convey a message, you need to also listen in a way that gains the full meaning of what's being said and makes the other person feel heard and understood.

***More than just the words you use, effective communication combines a set of 4 skills:***



- Engaged listening
- Nonverbal communication
- Managing stress in the moment
- Asserting yourself in a respectful way

While these are learned skills, communication is more effective when it becomes spontaneous rather than formulaic. A speech that is read, for example, rarely has the same impact as a speech that's delivered (or appears to be delivered) spontaneously. Of course, it takes time and effort to develop these skills. The more effort and practice you put in, the more instinctive and effective your communication skills will become.

**Common barriers to effective communication include:**

- Stress and out-of-control emotion.
- Lack of focus.
- Inconsistent body language.
- Negative body language.

Till now we have discussed about the behavioral aspect, now we will be elaborating the technical aspect and planning part of audit.

**Before Inspections:**

One way to stay abreast is to **check out 483s**, available online, to understand what sort of issues are being **identified by inspectors**. There are various resource centers, blogs and webinars that offer insight, including an FDA Inspections group on LinkedIn which share information about the latest inspection trends.

**Define roles for key employees** such as the Director of Quality, Regulatory Director, Quality Assurance Manager or Production Manager. Identify one employee to serve as the main liaison or company representative with the FDA inspector to **reduce any possible miscommunication**.

Make sure employees who get promoted get briefed on their **new responsibilities** and make sure backups are trained, in case a key executive is away.

Conduct regular training sessions to keep employees aware of the changes and best practices. You might even consider conducting a mock inspection to ensure people know how to deal with the **stress and strain** of a real inspection.



**Pre-Audit Preparation**

- Review key procedures like, Investigations, CAPAs, Complaints, Change Control, Product Release
- Review critical/major investigations- Ensure these have been adequately addressed.
- Review new equipment validations.
- Review critical/major complaints.
- Auditors often ask for a list of these investigations etc.- Can and should be prepared ahead of time.
- Don't forget about the previous audit response - ensure all actions were completed.
- A review of the major changes since the last audit
  - ✓ Validation protocols/reports.
  - ✓ Risk Assessments.
  - ✓ Change Control Forms.
  - ✓ Ensure they are reviewed and available in the war room!

**Keep in mind:**

That inspections can happen any time, so your personnel must be prepared at all times.

**At the Start of an Inspection:**

The inspection process generally begins when the FDA Inspector presents a notice of Inspection (FD-482) and proper FDA credentials. But employees should know whom to notify – and should contact that person immediately – if they are approached by an FDA investigator outside of normal business hours (i.e. after 5:00 p.m. and/or outside of the facility on the company grounds.

If the investigator does not present an FD-482 or credentials, the investigator should not be allowed to begin the investigation until you can authenticate the person's identity with FDA Field Operations. The company should make sure that all relevant managers and departments are aware that the FDA inspector is on the premises.

Typically requested ahead of time

- Current Site Master File.
- Procedures for deviation, OOS management & Change Control.
- List of significant changes since the last inspection.
- Validation Master Plan.
- Validation schedules for equipment, facilities, processes, methods and utilities.
- List of sponsors for whom testing of medicines is performed (testing lab requirement).
- List of test methods relating to the licence.
- Quality Metrics

While regular company business must continue as normal during the regulatory audit, audit coordinator like Corporate QA (CQA) or audit and compliance team should focus on the FDA inspection only.

There is a requirement for an empty conference room for the inspector to use as the base of operation while the inspection is being conducted, to review records.

The company representative will need to provide adequate time for a brief company orientation and allow time to answer any other questions the inspector may have in order to conduct the Investigation. The representative should escort the investigator(s) on any tour of any areas of the facility.

**Keep in mind:**



Facility inspections are designed to determine that cGMP standards are being met and that you are maintaining **appropriate records**. In any interaction with the inspector, employees should be **cooperative and avoid conflict**.

It is important to maintain the **right attitude**; rather than grumble to the inspector about the disruption – since the inspector is just doing his or her job – think of this an opportunity to show that your company is meeting or exceeding cGMP standards. If you're not sure what the inspector is requesting, **don't guess: Ask for clarification**.



Identify personnel likely to be involved in the audit

- Presenters – Primary Contact,
- Area-specific presenters,
- Reception,
- People to be in the audit room (this should be limited),
- Note takers,
- Runners,
- People for the 'war room' (prep area).

**During an FDA Inspection:**

The company representative should determine from the investigator the scope and purpose of the inspection. This allows the company to organize the visit properly to determine the approximate length of time the inspector will need to be on site.

During the visit, the inspector will need to do a proper document review, conduct appropriate interviews, and other inspection activities.

Company policies and procedures that will or may have an impact on the inspection should be reviewed with the inspector, including:

- Access to restricted areas.
- Restricted behaviors including the wearing of lab coats (in required areas).
- The absence of food or eating in animal labs.
- Any policy prohibiting the use of cameras, tape recorders or other audio and/or photographic equipment.
- Requests for copies, materials, and/or drug samples must be made through the company representative.

**Keep in mind:**

The inspection usually involves a combination of physical plant inspection and document and record review, including complaints, production records, QC records and storage and shipping

records. The investigation may also explore into procedures related to equipment and process controls and vendor and design specifications.

The company should keep a detailed record of dates, times, areas inspected, observations made, questions or remarks by the FDA inspector, and responses or remarks by any employee during the inspection. Duplicate copies of all material provided to the investigator should be retained by the company.

During the Inspection, the company representative should request that the investigator(s) identify areas, procedures, or documents which are judged as not good practices. That way, the company can address and correct the issue during the inspection. The company should demonstrate the inspector that the practices are now in compliance.



Meanwhile company should assessed by implementing the changes or recommendations does not impacting the quality of previously manufactured products.

At the end of each day of the inspection, after the FDA inspector has left the facilities, senior management should apprised the team. If there were any issues identified by the inspector, the managers of the impacted department should, when practical, prepare and implement the appropriate corrective preventive actions.

If an issue has been corrected during the inspection, we should ask the inspector to review the corrective actions at the start of the next inspection day. The goal is to close out all non-compliances prior to the completion of the inspection. This demonstrates the company's commitment to quality and provide it with the opportunity to review the proposed corrective action with the inspector and make any corrections should the inspector feel the corrective action did not resolve the issue.

*Information and Drug Sample Requests:*

When copies of records or documents are requested, company personnel should be the ones to make copies. FDA personnel should not be allowed to make copies nor should they take or write on the original data or documents.

All materials given to the investigator must be marked “Confidential” and/or “Proprietary,” and should be documented and listed by document title and number. The company should maintain a complete set of copied records and reports.

Requests for access to and copies of records and reports related to pre-clinical and clinical data conducted under the provisions of an IND are permitted under FDA authority.

No raw data or original documents may be taken off-site. The original documents should not be written on by the investigator.

Raw material, product samples or any other samples provided to the inspector should be listed by name, lot or batch number, and quantity on the FDA form (FDA 484). The company should retain a triplicate sample from the same lot for confirmatory testing. After the inspection is completed, a Freedom of Information (FOI) Request should be made to the FDA laboratory for a copy of its test results. The company may bill the FDA for samples taken.

Actual labels and labeling, (e.g. package inserts) and packaging may be collected by the investigator. Duplicates should be collected for the Company Record of the Inspection.

The inspector may ask for customer names and shipping records of products sold. This information should be provided. However, complete customer lists should not be provided during a routine inspection since this is confidential business information.

**Exit Interview Protocol:**

Upon completion of the inspection, the inspector will present a written FDA form (FDA 483) that contains a list of any negative observations that constitutes violation of Food and Drug law.

The inspector is then available for an exit interview to review any notes including any 483s. The senior management should attend this meeting.

During the exit interview, the company should take extensive notes and make sure that its people understand the issues around all 483 items, and how to correct those issues. Don't be afraid to ask clarifying questions as appropriate.

Any preliminary verbal response to a 483 observation by the company should be brief. It is not appropriate to vigorously argue a point with the FDA investigator during the exit meeting. However, if you feel a 483 observation is in error or the result of a misunderstanding or incomplete information, you should compile the proper documentation to support the company's position. If an issue remains unresolved, request the inspector to annotate the FDA 483 and his Establishment Report to reflect the differences.

If corrective action on an observation has been taken during the course of the investigation, this should be duly noted during the exit interview.

**Post Inspection Protocol:**

The inspection is over but there may still be work to be done.

The company representative should prepare a written report and maintain a file of the subjects, operations, documents, and activities that were inspected and/or performed during the FDA inspection.

The file shall contain duplicate copies of all records copied and taken by the FDA inspector. The report shall be reviewed by senior management and maintained by QA and should contain the following:

Reference the date of inspection and name(s) of members of inspection team, reason for written response, response to each cited deficiency, including observations resolved/corrected during the inspection and observed by the Investigator(s), description of preventive and corrective action to be taken regarding each observation for those items not resolved at the

time of written response and a schedule for completion, items still in dispute between the company and the FDA shall be addressed with necessary supporting information and documentation.

The Quality or Regulatory Director should submit the written response to the FDA within 10 working days of the exit interview.

After the inspection, the FDA inspector will write a narrative report called the Establishment Inspection Report (EIR). The Quality Director should submit a Freedom of Information (FOI) request for both a purged (confidential information removed) and an unpurged copy of the EIR. This should be sent directly to the FDA Freedom of Information Office in Rockville, Maryland.

The Quality Director should review all information received from the FDA after the inspection and coordinate all communication with the FDA. Any incorrect information should be communicated in writing to document the company's position.

**Conclusion:**

There are a lot of steps to ensure a successful FDA inspection. The most important is to ensure your facility implements current compliance procedures. Building on that, you need to develop and test your inspection plan, and train your employees so that everyone understands his/her role for before, during and after an inspection. Inspections can be a hassle but they are necessary to ensure the public safety.

With a detailed, thoughtful approach, you will be in a better position to pass inspections with a minimum of disruption.

## **FAQ: Question and answer**

### **What does the FDA inspect for?**

The Food and Drug Administration (FDA) conducts careful inspections of regulated facilities to determine a firm's compliance with regulations and the Food, Drug and Cosmetic Act. Inspections are one of many ways FDA protects the public health.

### **What is an FDA 483?**

An FDA Form 483 is issued to firm management at the conclusion of an inspection when an investigator(s) has observed any conditions that in their judgment may constitute violations of the Food Drug and Cosmetic (FD&C) Act and related Acts.

### **What is the FDA Form 482 for?**

FDA may conduct an inspection of your operation for a variety of reasons, such as a routinely scheduled investigation, a survey, or a response to a reported problem. The investigator will present credentials and "Notice of Inspection" (FDA Form 482) upon arriving at your plant.

### **Why is the FDA important?**

FDA Mission. The Food and Drug Administration is responsible for protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices; and by ensuring the safety of our nation's food supply, cosmetics, and products that emit radiation.

### **What is the purpose of an FDA warning letter?**

FDA warning letter. ... Typically, a Warning Letter notifies a responsible individual or firm that the Agency considers one or more products, practices, processes, or other activities to be in violation of the Federal Food, Drug, and Cosmetic Act (the Act), its implementing regulations and other federal statutes.

### What is an EIR from the FDA?

An FDA Form 483 is issued to firm management at the conclusion of an inspection when an investigator(s) has observed any conditions that in their judgment may constitute violations of the Food Drug and Cosmetic (FD&C) Act and related Acts.

### How does FDA classify inspection reports?

NAI – No action indicated

VAI – Voluntary action indicated (some deficiencies identified but not serious).

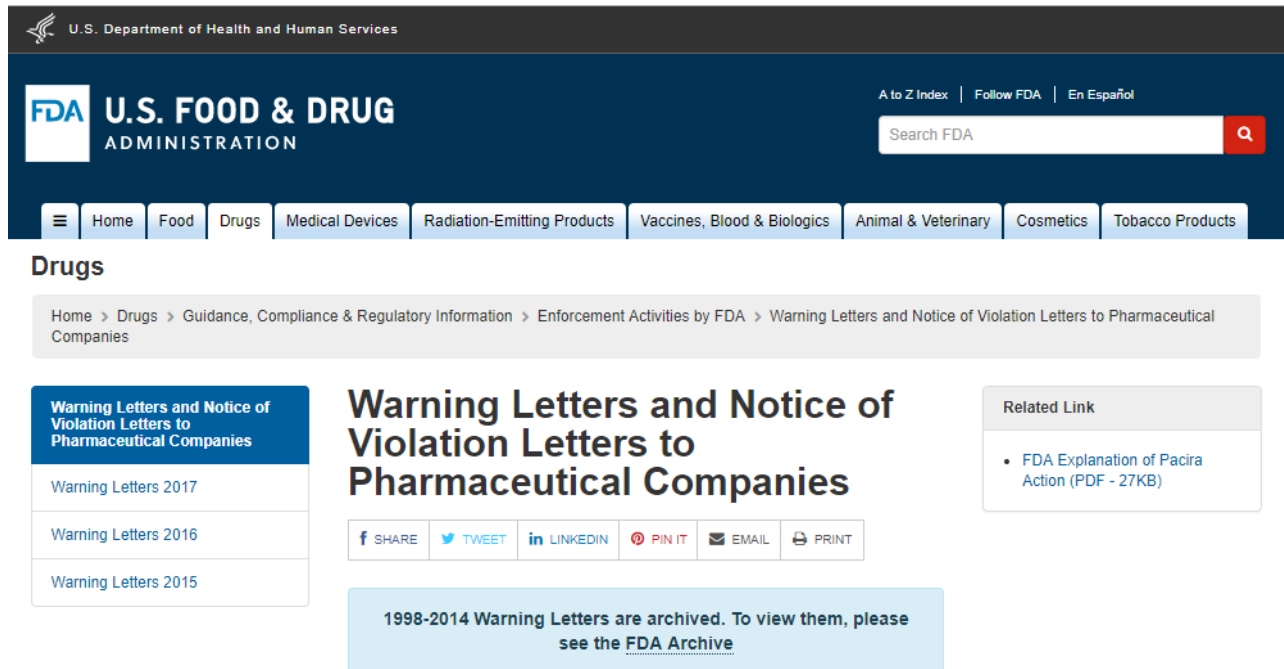
OAI – Official action indicated (serious deficiencies identified, and FDA must take action to assure correction).

### Where you get information regarding all warning letters issued by FDA?

It is a free online resource, available at

<https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/WarningLettersandNoticeofViolationLetterstoPharmaceuticalCompanies/default.htm>

Screen shots are shared below for ready references,



### What should I expect during an inspection?

FDA may conduct an inspection of your operation for a variety of reasons, such as a routinely scheduled investigation, a survey, or a response to a reported problem. The investigator will present credentials and "Notice of Inspection" (FDA Form 482) upon arriving at your plant. A knowledgeable person in your firm, such as the plant or production manager, preferably designated ahead of time, should accompany the investigator at all times. It is in your best interest to fully understand FDA's inspection procedures. When you are unsure of certain actions taken by the investigator, don't hesitate to ask questions.

Usually, the investigator will examine your production process, look at certain records and collect samples. At the conclusion of the inspection, the investigator will discuss with your firm's management any significant findings and concerns; and leave with your management a written report of any conditions or practices, which, in the investigator's judgment, indicate objectionable conditions, or practices. This list of "Inspectional Observations," also called an FDA Form 483, can be used by your firm's management as a guide for corrective action, since the FDA representative will not usually recommend specific corrective measures. Your firm can and should respond to the FDA-483 during the discussion with the investigator. In fact, corrective actions or procedural changes that were accomplished immediately in the presence of the investigator are regarded as positive indications of your concern and desire to voluntarily correct discrepancies.

If you do not agree with the actions being taken by the FDA or if you have a question about the jurisdiction of the agency in a particular matter, you can contact the FDA's Office of the Ombudsman to seek a resolution.

FDA Office of the Ombudsman,  
10903 New Hampshire Avenue

WO 32, Room 4231

Rockville, MD 20903

Telephone: 301-796-8530

FAX: 301-847-8628

E-mail: [ombuds@oc.fda.gov](mailto:ombuds@oc.fda.gov) (sending confidential information by electronic mail is not recommended)



**❖ Free Online Resources**

FDA Inspection guides available on the following mentioned link,

<https://www.fda.gov/ICECI/Inspections/InspectionGuides/default.htm>

Guidance document available under this section are mentioned below,

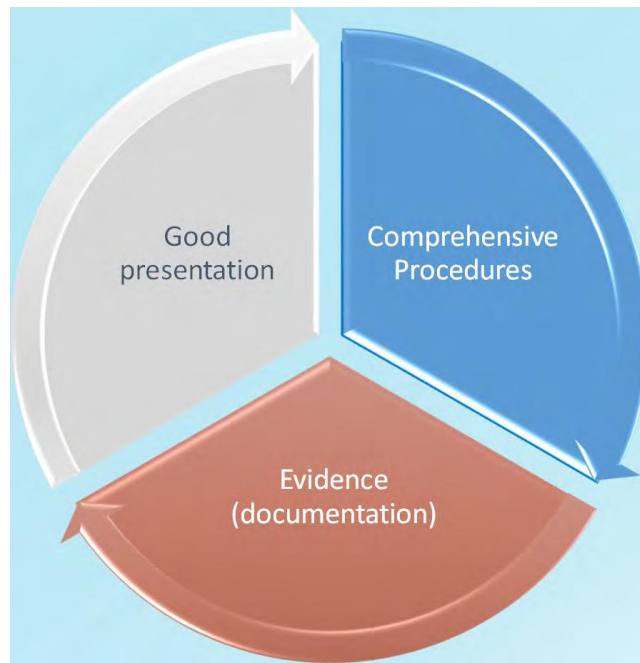
- [High Purity Water System \(7/93\)](#)
- [Lyophilization of Parenteral \(7/93\)](#)
- [Microbiological Pharmaceutical Quality Control Labs \(7/93\)](#)
- [Pharmaceutical Quality Control Labs \(7/93\)](#)
- [Validation of Cleaning Processes \(7/93\)](#)
- [Dosage Form Drug Manufacturers cGMPs \(10/93\)](#)
- [Oral Solid Dosage Forms Pre/Post Approval Issues \(1/94\)](#)
- [Sterile Drug Substance Manufacturers \(7/94\)](#)
- [Topical Drug Products \(7/94\)](#)
- [Oral Solutions and Suspensions \(8/94\)](#)
- [Computerized Systems in Drug Establishments \(2/83\)](#)

Note: These documents are reference material for investigators and other FDA personnel. The documents do not bind FDA and do not confer any rights, privileges, benefits or immunities for or on any person(s). An alternative approach may be used if such an approach satisfies the applicable statutes, regulations or both.

**References:**

<http://www.pharmacompliancemonitor.com/best-practices-handling-fda-inspections/7936/>

<https://www.fda.gov/ForIndustry/FDABasicsforIndustry/ucm237624.htm>



***Success in any audit require 3 things***



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