Preparing for Regulatory &/or Customer Compliance audits.
The aim of any audit

Assess compliance of a facility, its processes and procedures.
Ensure they are under adequate control.

Auditing is 90% preparation

The same can be said about being audited!
Preparation should be a constant state!
Before closing any report, investigation etc, ask -
would I be comfortable handing this to an auditor?
Be honest with yourself.
Any doubts – it’s incomplete.

Primary objective of an auditee:
Demonstrate compliance and control.
Initial Contact – First Steps

• Initial notification: Typically ~ 1-2 months beforehand.
  • unannounced inspections can be performed where required.

• Block out schedules – ensure key personnel are available.

• Does your company have a procedure for GMP audits?
  • Useful for unannounced audits – details key contacts, phone numbers etc

• 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).
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.
Do Your Research!

- Check if there is any information available on the auditor
  - FDA warning letters (for US inspectors)
    - Can indicate what an auditor likes to focus on.
    - Can indicate their background/training.
      - People naturally gravitate towards their comfort zone.
      - Where other companies fell down.
  - Other contacts within the industry/Seminars
    - Is there a particular (current) focus from a regulatory body?

- Regulatory updates
  - These shouldn’t be a surprise!
  - Ensure you have fully implemented any new regulations.
  - Ensure you are prepared for any upcoming regulatory changes.
    - Auditors will like to see early implementation of changes.

- Review the last audit report
  - Ensure all actions have been closed.
The FDA has publicly available guides for investigators and other FDA personnel: [http://www.fda.gov/ICECI/Inspections/InspectionGuides/default.htm](http://www.fda.gov/ICECI/Inspections/InspectionGuides/default.htm)

These can be useful for preparation, investigations and risk assessments.
# Drugs

- 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)

# Foods & Cosmetics

- Allergy Inspection Guide (4/01)
- Aseptic Processing and Packaging for the Food Industry
- Nutritional Labeling and Education Act (NLEA) Requirements (8/94 - 2/95)
- Computerized Systems in the Food Processing Industry
- Grain Product Manufacturers
A Risk-Based approach is used by the TGA for scheduling re-audits.

There is also a schedule for medical devices.
Level A1 = Good
No ‘major’ deficiencies or non-conformities were found, which are of a relatively minor nature.

Level A2 = Satisfactory
1 to 5 major deficiencies and/or a larger number of minor deficiencies or non-conformities were found.
No critical deficiencies were found.

Level A3 = Basic
6 to 10 major deficiencies and/or a large number of minor deficiencies/non-conformities were found.
No critical deficiencies were found.

Not rated = Unacceptable
1 or more critical deficiencies and/or > 10 major deficiencies were found.
Preparation

- Review key procedures
  - 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.
Preparation

- One of the first items:
  - 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!

- Identify key exposures within each area
  - List exposures (team brainstorming sessions).
    - Include a review of completed investigations, new product introductions,..
  - Prioritize major/critical exposures.
  - Agree actions.
  - Assign responsibility & timelines for each action.
  - Periodic review & progress updates
    - Move resources if needed
  - Assess the need for ‘Position Statements’.
    - Typically prepared where gaps cannot be addressed.
Success in any audit requires 3 things

- Comprehensive Procedures
- Evidence (documentation)
- Good presentation
• The importance of good presentation
  • You can’t make a bad system look good.
  • You CAN make a typically good system look bad.

Examples:
  • Notice boards with operational details present
    • Trend data may lead an auditor to issues.
    • Remove all unnecessary information.
  • Poor housekeeping.
  • Obvious non-compliances on the tour.
    • An inspection is not the time to find these.
  • Unprepared or poor/non-versatile presenters.
Selecting Your Presenters

- Identify subject matter experts in each area
  - Important: identify back-up presenters
    - Auditors may split up or primary presenter unavailable.
  - They should be involved in pre-reviewing procedures for currency.

- Should be comfortable answering questions.
  - Don’t select a quivering mass of indecision!

- Typically presenters are managers or team leaders
  - General employees may also be questioned.
Who makes the best presenter?

- The spin doctor
- The defence lawyer
- The mute

The ideal presenter must be all three! - Versatility

Spin-doctor: Pleasant, confident & promotes all that is good in the system.

Defence lawyer: Must reassure the inspector of the system capability e.g. redirecting to other procedures if necessary.

Mute: You must know when to stop talking.
Training – Responding to Questions

• Train the presenters:
  • to understand the audit process,
    • to ‘not panic’ when it changes suddenly.
  • to cope with difficult & unexpected questions,
  • remind them that they can refer to procedures,
    • Do not guess.

• How to effectively answer questions:
  • Answers should be
    • Complete.
    • Truthful.
    • Concise – with no additional information.
Training – Responding to Questions

Do you have the time?

Typical answer – “It’s 11:45”

Volunteers more information than was asked for!

This also applies to providing documentation!
Training – Auditing Techniques

• The different techniques used by inspectors.
  • Open ended requests..
    “Describe the procedure to me.”
  • The silent treatment.
    Don’t feel the need to speak first!

• Different starting points/audit types
  • Finished Product (backwards/top-down)
  • Raw materials (forwards/bottom-up)
  • Major investigations
  • Major changes
  • Complaints
  • CAPAs
Training - Audit Etiquette

- Be polite and helpful.
  - Don’t be obstructive.

- Accept citations.
  - Don’t argue.
  - You can present your case to a point.
  - Know when to stop!

- Let the ‘Presenters’ present.
  - Don’t offer answers for areas where your knowledge is limited.
Conduct Mock Audits

- Can help to identify compliance issues.
- Familiarize employees with the process.
- Enable employees to practice how best to answer questions.
- External auditors – less familiar but may be useful.
  - If internal staff are not experienced.
  - Preparation for an initial license application.

Note: more than one should be planned if possible.
Preparations for Audit Day

- Key things to address:
  - Who to notify when the auditor arrives on site.
  - The location of the audit room.
  - Who will be present at the opening meeting.

- The tour route.

- Any site specific H&S issues which the auditor needs to know about.
  - Suitably sized coats etc available.

- Assembling any information requested by the auditor (if not already communicated to them).
War Room

Primary function - support for presenters.

• Ensure it is adequately resourced
  • Getting requested documents.
  • Tracking location of the auditor.
  • Holding documents likely to be requested.
  • Documenting requested information & if it has been presented.
  • Reviewing documents prior to their presentation.
  • Area for presenters to wait.

• Establish communication channels for key personnel.
A log should be set up for

- All documents requested by the inspectors,
- removed and/or requested from archives, QA etc..

You need to make sure they go back after.
The log can help to prepare for future audits.
Thank You
Useful Links & References

TGA Inspection Process:  

TGA examples of medicine inspection deficiencies:  

TGA Re-Inspection Timetables:  

FDA Warning Letters:  
http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/default.htm

FDA Inspection Guides:  
http://www.fda.gov/ICECI/Inspections/InspectionGuides/default.htm

Inspection Readiness: A Guide to Preparing Subject Matter Experts to Face the FDA  
Useful Links & References

US FDA - Investigations Operations Manual, Chapter 5 - Establishment Inspections:
http://www.fda.gov/ICECI/Inspections/IOM/default.htm

Guidelines for Regulatory Auditing of Quality Management Systems of Medical Device Part 2: Regulatory Auditing Strategy:
http://www.fda.gov/ohrms/dockets/dockets/06d0011/06d-0011-gdl0001-Tab-11.pdf

International Regulatory Audits for Pharma:
http://www.pharmacompliancemonitor.com/international-regulatory-audits-for-pharma/1704/

Preparing your analytical lab for a regulatory audit:
https://www.chem.agilent.com/Library/eseminars/Public/Preparing_Your_Analytical_Lab_For_A_Regulatory_Audit.pdf

How to plan for a GMP audit in Pharmaceuticals:
http://www.pharmaguideline.com/2013/10/how-to-plan-for-gmp-audit.html

Planning and procedure followed during regulatory audits:

White Paper – Preparing for GMP audits:
http://www.pharmout.net/downloads/index.php#whitepapers

Auditing as a Component of a Pharmaceutical Quality System:
http://www.ivtnetwork.com/sites/default/files/AuditingComponent_01.pdf