

Tips on international ANVISA Inspections – RDC 59 / 2000 – Good Manufacturing Practices

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ANVISA's inspection

- Based on Brazilian GMP regulation RDC 59/2000 and checklist
- Pre scheduled by ANVISA: importer and manufacturing site agreement, duration one week
- Always 2 ANVISA's inspectors

ANVISA's inspection

- Follows an agenda:
 - Opening meeting
 - Inspection: facility visiting, including third party (final assembling if the case)
 - Document review
 - Wrap up meeting: opportunity for last clarifications or to show conformity

ANVISA's inspection

- After inspection, a report is generated concluding 1 or 2 below
 - 1 - Meets GMP requirements: a certificate will be issued
 - 2 - Does not meet GMP requirements: a certificate only will be issued after compliance evidence of observations (checked by re inspection or data submission depending on the case)

Preparing for the inspection

- Regulation and checklist in English
- Site personnel training
- Some focus on Part G requirements

Preparing for the inspection

- Confirm availability of experts, system and documentation
- Verify past recalls or adverse events
- Verify audits of critical suppliers

Working with ANVISA`s Inspectors

- The Audit Host is the primary contact for the company and the inspection coordinator
- The host will assure that proper personnel are present during questioning

Working with ANVISA`s Inspectors

- It cannot be stressed enough the need of the presence of a Brazilian employee (in the case of manufacturers which have offices in Brazil) or another Portuguese-speaking individual
- It's strongly advised that the 'accompanying Brazilian agent' has good communication skills and knowledge/thorough knowledge of
 - the Brazilian regulations
 - the auditee Quality system

Working with ANVISA`s Inspectors

- The “Brazilian agent” will accompany the ANVISA inspectors full time and provide facilitation between the site representatives and ANVISA inspectors, in particular related to translation and how to behave during the inspection
- He also should perform a pre-visit of the inspected area, if possible, during the preparation for the inspection

Working with ANVISA`s Inspectors

- Subject matter experts will accompany the inspector under the direction of the inspection coordinator and Brazilian agent
- SME's are selected for their area of expertise and will respond to area specific questions from the inspector

Working with ANVISA`s Inspectors

- SME's will be briefed by the inspection coordinator and Brazilian agent on:
 - anticipated line of questioning
 - expected behavior, do's and don'ts
 - exercising tact and diplomacy

Working with ANVISA`s Inspectors

- Strongly suggested rules
 - No cameras or tape recorders on either side
 - Limit as much as possible inspector access to company software or company computers
 - Inspector must ALWAYS be accompanied by Brazilian agent

Working with ANVISA`s Inspectors

- Strongly suggested rules
 - Inspector not allowed to mark company documents
 - Only Host or QA Representative to sign documents, other site personnel not allowed to sign ANVISA`s documents
- Strongly recommended front office/back office system

Working with ANVISA`s Inspectors

- All items of the regulation will be verified, however, some will be verified in more detail depending on the background of the inspector

Most discussed topics

- Focus on SOPs and documentation
- Personnel & organization
- Design controls
- Device validation
- Document control & records
- Supply chain procedures
- Traceability & identification
- Manufacturing process control

Most discussed topics

- Tests and product release/rejection
- Training
- Packaging and labeling controls
- Internal audits
- Housekeeping
- Complaint Handling
- CAPA

Inspection “Do’s” - General

- Be pleasant, hospitable, business like, respectful – first impressions can influence the mood of the inspection
- Be honest – always tell the truth when answering questions
- Be prepared – have main documents/information easy to reach and present

Inspection “Do’s” - General

- When answering questions,
 - Try and be direct & concise, do not answer beyond the scope of the questions
 - Seek clarification if needed from host and/or inspector
 - Do not offer unsolicited comments
 - Have assurance of the answers – do not guess
 - Do not express personal views and opinions

Inspection “Do’s” - General

- Avoid generalities - words like “typically”, “generally”, “usually” and “most of the time” These responses only invite more questions
- Try and be comfortable with silence
- Try and be responsive and be sure you understand the information requested

Inspection “Do’s” - General

- Be confident in your Quality system – but not over confident. It is good to be proud but it is bad to be arrogant

Inspection “Don’ts” - General

- Answer the questions accurately, factually, and to the best of your knowledge
- Do NOT argue: if it’s feasible, just do what is said (even if it is not on check list). If it’s unfeasible, make your point in a polite way
- Don’t blame some other organization

Inspection “Don’ts” - General

- Don’t admit you had a problem and did nothing
- Don’t refuse to show requested information
- Don’t state that a particular event is impossible – the inspector may have a report that covers this event

Inspection “Don’ts” - General

- Don’t break the inspector’s silence
- If the inspector asks for an example, **don’t give the whole book** – you are inviting a “fishing expedition”
- **Don’t take books of notes or other non-essential papers or things into the Front Room** – the inspector will want to look at them...

Inspection “Don’ts” - General

- The manner in which questions are answered is very important
 - Don’t be defensive
 - Don’t “clam up” – saying nothing is as bad as saying too much
 - Don’t appear to be concealing information

Inspection “Don’ts” - General

- Don’t imply difficulties or problems are linked to or caused by a lack of resources
- Don’t bring in cell phones/ pagers ... shut them off ... or put on vibration
- Don’t use “internal” acronyms or terminology
- Don’t compare ANVISA to other agencies, particular FDA

Do's for Front Room Hosts and Back Room Managers

- Make sure **people are available when needed** as this can influence the climate of the inspection
- Make 2 copies of everything – 1 for the inspector and one for the site files
 - Mark documents as “Confidential” unless they are available to the public
- **Make corrections or updates as needed during the inspection**

Do's for Front Room Hosts and Back Room Managers

- Take good notes of
 - What was inspected/when, areas of interest
 - Key questions/answers, comments on adequacy/inadequacy
 - Documents & records reviewed, key points of discussions
 - List of any samples taken

Don'ts for Front Room Hosts and Back Room Managers

- Don't bring a lawyer unless some clarification is needed!
- Don't sign affidavits, forms, or initial changes on a non-company document. Let the audit hosts handle these requests
- Don't have everybody speak to the inspector, limit the number of people the inspector talks to
- Don't leave the inspector alone to wander and interview outside of Host control

What to provide to ANVISA's inspectors

- DO:
 - Coffee, Tea, Work Lunch and Water
 - A private work area if requested
 - Access to a copy machine, phone and fax
 - Visitor parking spaces
 - Common Courtesy

- DO NOT:
 - Pay for meals
 - Offer any gifts

What to provide to ANVISA's inspectors

- You can socialize after work hours if inspector wishes, like sightseeing or having a dinner in the same restaurant
- Also is recommended Brazilian agent to stay at same hotel and use same transportation service to get in and out of manufacturing site

Additional information

- Front room (audit coordination)
 - SME's are selected for their area of expertise and will respond to area specific questions from the inspector
 - Understand the regulation checklist, anticipate questioning and areas to be checked

Additional information

- Site visit
 - Have a defined route
 - Guarantee that the group will be together during the visit
 - Examples of DHR – device history record and procedures available
 - Availability of systems

Additional information

- Back room (evidence preparation room)
 - Experts must be available
 - Prepare inspection evidence
 - Procedures according to ANVISA checklist
 - Examples of records which show adherence to procedures
 - Someone should track the inspection checklist to anticipate actions

Additional information

- Manufacturing
- Ensure that personnel are following the correct procedures
- Show how materials and components are treated and segregated
- Equipment calibration
- Cleaning and general organization – fundamental points
- Pest control

Thanks!

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