Session 10:

The UNFPA Prequalification Site Inspection

World Health Organization

UNFPA

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A catalyst for global health

Group Brainstorm: Site Inspection

- In your experience, in what areas have you disagreed with the inspectors?

Objectives

- Provide overview of what inspectors are looking for during a site inspection
- Discuss strategies for overcoming site inspection problems

Inspectors could look at…..

EVERYTHING

that may affect the quality of the product

What Inspectors Are Looking For

- Good infrastructure and environment
- Good equipment in good condition
- Competent staff
- Quality control (QC) system that provides early warnings
- Appropriate corrective action
- Documented policies, procedures, records of production, and testing
- Consistent production of good-quality product

Actual Scope of Inspection

- Assess ALL parts of the production process
- Inquire more deeply into possible sources of quality problems
- Look at procedures and records

Site Master File and Product Dossier

- Inspectors will have copies before visit
- May concentrate on select matters based on document content
- Inspectors will document inconsistencies between documents and factory practice

What Is the Difference Between a UNFPA Inspection and an ISO 13485 Audit?

- UNFPA inspection is mainly technical
- Half the time is spent in factory or laboratory
- Looks at:
  - Selected aspects of ISO 13485
  - Suitability and state of equipment
  - Authority and responsibilities of key staff
- ISO 13485 audits focus on documentation

Initial Session

- Find out about the factory:
  - Capacity
  - Operating hours
  - Sales
  - Key staff and responsibilities
  - Independent certifications

Raw Materials: Group Question

- From your experience in site inspections, what issues have been covered with regard to raw materials?

Raw Materials

- Selection of raw materials and suppliers
- Testing/acceptance of raw materials
- Storage conditions
- Identification of accepted, rejected, and unassessed material
- Orderly usage
- Records of raw materials and their use

The Production Process

- Are there written procedures for all activities that may affect quality?
- Is there a system to ensure that these are updated and kept in an orderly way?
- Does the factory follow the procedures?
- Are records kept of process conditions?

The Production Process
(continued)

- Are the staff in each section competent?
- Is the environment kept appropriately clean for the stage concerned?
- Is environmental testing done where necessary?
- Is staff hygiene and access control appropriate for each stage?

In-Process Quality Control: Group Question

- From your experience in site inspections, what issues have been covered with regard to in-process quality control (QC)?

In-Process QC

- What tests are done at each stage of the production?
- What are the sample sizes, and how often are the tests done?
- How exactly are the results used?
- Are the tests well chosen, and are the resulting actions appropriate?

In-Process Testing

- Raw materials
- Dispersion
- Compounded latex
- Dip tank latex
- Dipped product
- After-processing
- After-ET
- Foiled product

Shelf Life

- Depending on information provided in Product Dossier, inspectors may seek more detail
- May look at shelf life data
- May look at how samples were kept

Batch (Lot) Documentation

- From the batch number, can the factory:
  - Identify all the sublots used?
  - Identify all the machines used to produce, test, and pack the products?
  - Know the process conditions at the time of manufacture?
  - Know which compound and raw materials were used?
  - Retrieve test results from all stages?

  AND demonstrate how they keep the information?

The Quality System: Group Question

- From your experience in site inspections, what issues have been covered with regard to quality systems?

The Quality System

- Must have a documented quality management system
- Will require ISO 13485
- Documented system must match what is actually done
- Amendments to the system must be recorded correctly

Quality System Documentation

- How is it organized?
- What language(s) is it in?
- Are factory operating procedures:
  - Correct?
  - Readily available to the operators?
  - Understandable by the operators?
  - Followed by the operators?

Use of Statistics

- Are test results used appropriately to make decisions about process or sublot?
- Is data used for trend analysis and early warning?
- Are final release tests done with the right sample sizes and decision rules?

Maintenance

- Is there a program for preventative maintenance?
- Are there procedures for preventative maintenance?
- Is the program followed?
- Are the procedures followed?
- Are records kept of preventative maintenance?
- Are records kept of breakdown maintenance?
- Does the factory use the records to modify the maintenance schedules?

Laboratories: Group Question

- From your experience in site inspections, what issues have been covered with regard to laboratories?

Laboratories

- Is lab equipment suitable for tests required?
- Is it in good condition?
- Does the staff perform the tests competently?
- Is the equipment calibrated at appropriate intervals?
- Are calibration certificates available and correct?
- How are test results recorded and stored?
- How are test results communicated to manufacturing?

Laboratories
(continued)

- Does the lab keep retention samples?
- If so, how and how many?
- Are the samples ever tested?
- Does the lab participate in interlab trials?
- Do they analyze interlab trial results?
- Does the staff have the necessary skills?
- Does the staff know the content of relevant standards?

Testing Issues

- Is the sample taken representative of the production?
- Is the test machine properly designed and installed?
- Is the test machine properly calibrated?
- Is the operator doing the test properly?
- Is the management capable of interpreting the results?
- If there are equivalent tests, do they give the same results?

What is Calibration?

Calibration

- Verifying that an instrument is measuring correctly *or*
- Adjusting the output of an instrument so it does measure correctly *or*
- Producing some correction factors so an instrument will measure correctly
- Calibration must be traceable to master instrument, preferably a national standard

Traceability

- National Standards labs: most accurate
- Accredited metrology laboratories: probably less accurate
- Labs doing internal calibrations: probably even less accurate

Human Resources (Staff)

- Are there enough staff members?
- Do the key staff members have appropriate skills and qualifications?
- How are staff selected?
- How are staff trained?
- Is there a training program?
- Are records of training maintained?

Infrastructure

- Is the building structure adequate?
- Is there enough space?
- What standards does process water meet, and how is it made?
- Is the compressed air quality and reliability adequate?
- Is electricity supply reliable? If not, how are interruptions handled?

Environmental Issues: Group Question

- From your experience in site inspections, what issues have been covered with regard to environmental issues?

Environmental Issues

- Is overall cleanliness adequate?
- Does waste disposal meet environmental standards?
- How is waste water handled?
- If there is a boiler, are emissions adequately controlled?

Independent Testing

- Factory records compared with results of independent testing
- Samples may be taken during the inspection or at a different time
- Physical testing will be done in accordance with Annex B of ISO 4074

The Inspection Report

- Closing meeting after inspection
- Main findings presented and discussed
- Full report, including description of factory and processes, combined with test reports sent to UNFPA

Possible Outcomes

- UNFPA will formally inform the manufacturer whether they:
  - Prequalify without conditions
  - Prequalify subject to specified corrective action
  - Requirement for corrective action and possible repeat site inspection
  - Determine site ineligible for prequalification

Continued Reporting for Prequalified Manufacturers

- Required to advise UNFPA within 2 weeks of any matter affecting information on which approval was based
- UNFPA may request reports from consumer, regulatory or other bodies regarding quality and supply of condoms
- UNFPA may periodically test samples from manufacturer

Site Inspection Guide

Areas listed below will be typically covered during the inspection which may be varied for different process flows and different materials usage.

Access to all documents and records related to the manufacture of specific male latex condoms as indicated in ISO 7034 and WHO Specifications will be required.

Areas under Inspection
1. General Company Detail Address and contact detail Condom designs manufactured Independent certifications-systems and products, including regulatory approvals. Markets serviced Operating hours and shifts
2. Management team and Key staff Review detail of management and key staff including authorities and responsibilities Organizational chart Review out of office hours responsibilities and authorities
3. Production capacities throughout the operation Number and type of machines Quoted output and yields Actual sales for past 3 years

4. Latex and other raw materials

Latex and other raw materials selection, storage and quality

Latex and other material and vendor evaluation/validation

Security of latex supplies

Acceptance and storage procedures

Status indication, labelling and documentation

Environment

5. Preparation of dispersions and compounds

Process

Adequacy of equipment

Testing and controls

Documentation and labelling

Environment

6. Latex pre-vulcanisation and maturation process and controls

Process

Adequacy of equipment

Testing and controls

Documentation and labelling

Equipment and process validation

Environment

7. Dipping

Process

Adequacy of equipment

Testing and controls

Documentation and labelling

Equipment and process validation

Environment

8. After processing (washing and powdering)

Materials Used

Process

Adequacy of equipment

Testing and controls

Documentation and labelling

Equipment and process validation

Environment

9. Electronic testing

Process

Adequacy of equipment

Testing and controls

Documentation and labelling

Equipment and process validation

Environment

10. Foiling Materials used Process Adequacy of equipment Testing and controls Documentation and labelling Understanding of lot coding Equipment and process validation Environment
11. Consumer/Customer Packing Materials used Process Adequacy of equipment Testing and controls Documentation and labelling Understanding of lot coding Environment
12. Warehousing Adequacy Segregation Labelling Stock control/rotation Presence of aged or non conforming goods

13. Quality Control Plan Detail of product testing throughout each stage of the manufacturing process including lot release Process yields throughout each stage of manufacture
14. Provisions for storage and control of work in progress
15. Outgoing Product Quality Review of process averages
16. Quality System and Documentation Quality manual SOP's and work instructions Documented versus actual practices Document control Contract review Risk review assessment and management Complaints, recall, vigilance and advisory notices Post market surveillance Internal audit Control of non conforming product Lot traceability Statistical analysis of collected data

17. Maintenance Documented program including schedule Detail of maintenance for key areas Records of maintenance Adequacy program
18. Laboratory Facilities, Competence and Calibration Routine activities of each lab Equipment and methods Reporting of results Documentation Calibration system Certifications Inter laboratory trial participation R&D activities Understanding and competence
19. Human Resources Staff numbers and areas of deployment Staff selection, induction and training systems Records
20. Shelf Life Stability Detail of studies conducted Retention sample program

21. Building, Grounds and Services
Overall fabric and condition of premises
Pest and rodent control
Compressed air
Process water quality
Effluent treatment
Electricity

Principles of Calibration

Purpose of calibration

The purpose of calibration is to give confidence that measurements are giving the correct result.

What is calibration?

Calibration involves one or more of the following processes:

- Verifying that an instrument is measuring correctly.
- Adjusting the output of an instrument so that it does measure correctly.
- Producing some correction factors so that an instrument will measure correctly.

Who does calibration?

Calibration is performed by:

- Labs that use the instruments.
- External "metrology" laboratories.

Basic principles

- The SI system of measurement has four fundamental units:
  - Mass
  - Length
  - Time
  - Electric charge
- All other units are derived from these.
- "Standards" for these units are held by national measurement labs.
- For convenience, standards for other derived units are also held.
- Accredited laboratories must be able to show that their calibrations are traceable to national or international standards.
- This is a step-by-step process.

Traceability

- National Standards labs may calibrate the equipment of others against reference instruments that are themselves calibrated against national standards (most accurate).
- Accredited metrology laboratories may use reference equipment calibrated by national standards labs (probably less accurate).
- Labs doing internal calibrations may have instruments calibrated against instruments held by metrology laboratories, and use these to calibrate instruments used on a daily basis (probably even less accurate).

Type 1 calibration

- The calibrating authority certification verifies that all readings are within *x*% of the true value, and that *x* is good enough for your purposes.
- If *x* is not good enough, then you have to send the instrument for repair or replace it with a new one.

Type 2 calibration

- The process of calibration actually adjusts the way the raw data is treated to give an output which is correct.
- Enersol's inflation tester, pH meters, and many spectroscopic instruments are examples of this.

Type 3 calibration

- The calibrating authority produces a table of instrument readings and the corresponding real values.
- The user of the instrument can then make appropriate corrections, if necessary.
- Alternatively, in simple cases, the calibrating authority may simply give a correction factor (additive or multiplicative).

Calibration points

- How many points are done depends on how thorough you want to be. In some cases, people do one-point calibrations (e.g., barometer). Generally, five to ten points are done for each instrument or instrument range.

Which points

- You can tell the calibration organization what you want.
- Make sure that the points used cover the part of the range you will use.
  - For example, if you measure thickness with a dial gauge, you are interested in the 0 to 0.2 mm range.
  - Any readings in the 0.5 to 12 mm range are not interesting for condom thickness.

How often?

- Frequency of calibration depends on the instrument and how it is used.
- Some accreditation agencies give recalibration intervals.
- In other cases, it is up to the lab to make its own judgment about the frequency of calibration.

When you get a certificate….

- Review it for plausibility.
- Compare it with the previous certificate.
- If you have any doubts about the certificates, consult the calibration company.