“QUALITY IS NOT AN ACCIDENT; BUT IT IS THE RESULT OF INTELLIGENT EFFORTS”

WHAT IS QUALITY?

- “Quality is fitness for use. ”
- “The totality of features and characteristics of a product or service that bear on its ability to satisfy a given need.”
- “Quality involves meeting customers need, preferences and exceeding it.”
- “Quality also encompasses people, process and environment.”

WHY QUALITY CONTROL?

- Manufacturing process is a repetitive process depending on both controllable and non-controllable factors.
- This produces deviation in the quality of the product.
- QC is the process of verification , or correction of the quality of the product when deviations are found to be more than expected.

WHAT IS QUALITY CONTROL?

"Those planned and systematic actions which provides a mean to control and measure the characteristics of a product, process or a service to established requirements."

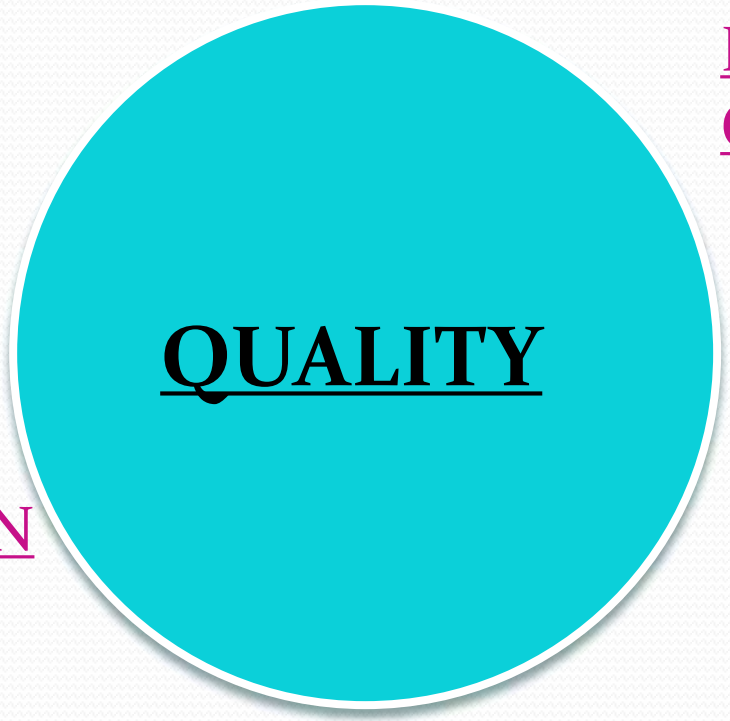
QUALITY CONTROL AS PER ISO:

- "The operational techniques and activities that are used to satisfy quality requirements."
- The quality control system verifies and maintains desired level of quality in an existing product or service by careful planning, use of proper equipments and continued inspection and corrective action as required.

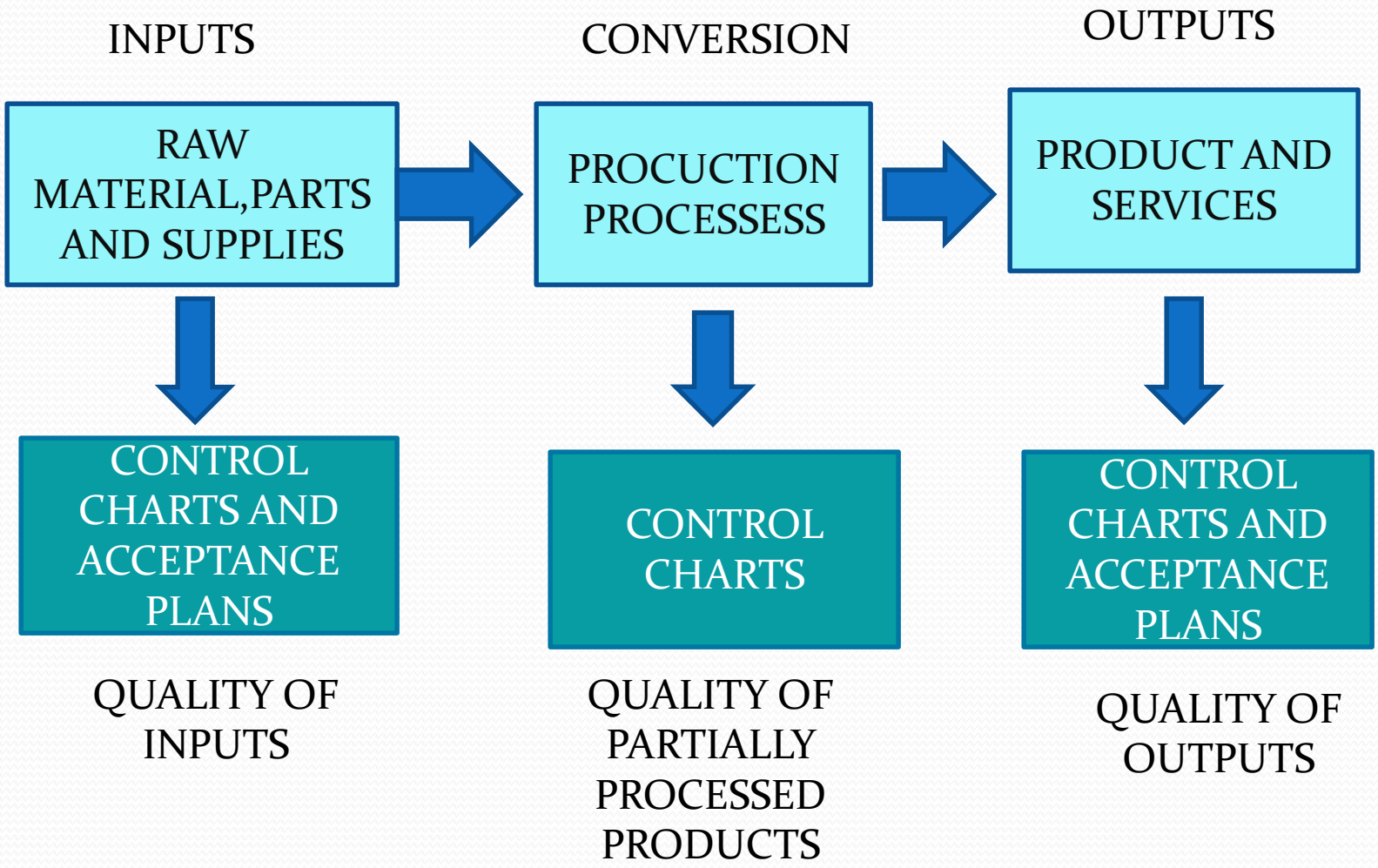
WHAT IS QC INSPECTION

- The ISO standard defines inspection as “activity of measuring, examining, testing one or more characteristics of a product or service and comparing the results with specified requirements in order to establish whether conformity is achieved for each characteristic.”

QC AND INSPECTION



QC THROUGHOUT PRODUCTION SYSTEM



PRE-PRODUCTION QC INSPECTION

- The safety and efficacy of the finished dosage form is largely dependent on the purity and quality of the bulk active drug substance.

- Physical tests such as particle size for raw materials flow properties etc. are essential tests to assure consistent operation of the production and control system and to assure quality and efficacy

PRE-PRODUCTION QC INSPECTION

- To decrease quality risk, the inputs can be inspected prior to production.
- Samples are randomly taken and checked.
- An experienced inspector examines the sample/prototype to make sure that

✓ the raw materials meet the specified standards

✓ Whether development team has clearly communicated the requirements to the manufacturing team.

✓ Whether equipments for mass production is similar to that for making prototypes.

IN PROCESS INSPECTION

- The first products that got out of the line are inspected for conformity.
- If issues are raised at this stage, the factory can immediately take actions and avoid delays.
- In-process products are rarely checked as it takes technician to reliably detect errors on unfinished products.

IN PROCESS QC INSPECTION

- Inspect the test results from in-process tests performed for conformance with established sampling and testing protocols, analytical methods, and specifications.
- For example, evaluate the tests for weight variation, hardness, and friability. All testing must comply with cGMP.
- The inspection must confirm that the in-process tests were done, as described in the plan, and ascertain that the results are within specifications.

CLASSIFICATION OF IN-PROCESS INSPECTION

1. Trial run inspection: Tools and machines are checked before operation.
2. First-off inspection: The items produced in the first production run are inspected and examined with respect to specifications.
3. Inspection by self control: Done by operators, controlling operations at different levels of production process.
4. Decentralised inspection: Semi finished goods are inspected either on machines or in the production line.

5. Centralised inspection:

- There can be single inspection unit for whole plant
- Or each section can have inspection unit to inspect the items
- The inspection staff is more experienced and skilled in this case
- Sophisticated and reliable instruments and techniques are use to measure the quality
- Hence centralised inspection is reliable and accurate.

QC INSPECTION IN PRODUCTION

1) Component dominant: Incoming material must be checked for required specifications.
2) Set-up dominant: An operation once set at a level, remains at that level for long. Hence products produced initially if found free from defects and conforming to specifications, then the operation can be cleared for continuous operation.
3) Machine dominant: Operation drift away from initial set-up level as operation proceeds. Hence needs periodic inspection for correcting set up.

4. Operator dominant: A certain portion of job is entirely influenced by operator's skill.

5.Information dominant: All the information including the SOP's, nature of job is given to concerned person.

6.Record dominant: The written records and documentation of every process and test conducted should be maintained.

QC INSPECTION IN ANALYTICAL

In general, these inspections include:

- The specific methodology which will be used to test a new drug product
- A complete assessment of laboratories conformance with GMP'S
- A specific aspect of laboratory operations

- Laboratory records and logs represent a vital source of information that allows a complete overview of the technical ability of the staff and of overall quality control procedures.
- SOPs should be complete and adequate and the operations of the laboratories should conform to the written procedures.
- Specifications and analytical procedures should be suitable and, as applicable, in conformance with application commitments and compendial requirements

- Documents relating to the formulation of the product, synthesis of the bulk drug substance, product specifications, analysis of the product, and others are examined during the review process in headquarter
- Inspections are designed to determine if the data submitted in an application are authentic and accurate and if the procedures listed in the application were actually used to produce the data contained in the application.
- Additionally, they are designed to confirm that plants (including QC laboratory) are in compliance with CGMP regulations.

FDA INSPECTION

- Based on team inspection approach.
- Highly technical and specialised testing equipments, procedures, data manipulations as well scientific laboratory operations will be evaluated.
- The inspection of a laboratory requires the use of observations of the laboratory in operation and of the raw laboratory data to evaluate compliance with CGMP's.

FDA INSPECTION- 4M's

1. MACHINE:

- ✓ Inspection should confirm that preventive maintenance, cleaning, adjustment etc are performed

- ✓ Machine usage, maintenance, calibration logs, repair records should be examined

- ✓ Verify that the equipments were in good working order at the time the batches were analysed.

2. METHOD/PROCESS:

- ✓ Information regarding validation of methods should be carefully evaluated
- ✓ All processes that may cause deviation to a device's specification and all validated process must be monitored and controlled
- ✓ If the process is software controlled, confirm that the software was validated
- ✓ Review the software documents, software validation activities, software change controls and software validation results to confirm that software will meet user need

3. MATERIALS:

- ✓ Raw material testing is of utmost importance as it directly affects the quality of final product
- ✓ Hence inspection should examine the analysis of materials including purity test, quality, charts etc
- ✓ Inspect if the methods for analysing the purity were validated
- ✓ The manufacturer must have complete knowledge of manufacturing process and the potential impurities that may appear in materials.
- ✓ These impurities cannot be evaluated by without a suitable method and one that has been validated

4. MAN:

- ✓ Verify that personnel have been qualified to implement validated processes or
- ✓ appropriately trained to implement processes which yield results that can be fully verified
- ✓ Confirm that the employees have complete knowledge of the devices, processes
- ✓ Confirm that employees are aware of the device defects that may occur as a result of improper performances
- ✓ Confirm that the employees conducting QC tests are aware of the defects and errors that may be encountered while performing their responsibilities

FINAL INSPECTION

- It is also known pre-shipment inspection.
- This is the most popular type of QC inspection for importers.
- It takes place once all the products are finished and ready for shipment.
- The samples are drawn in a random manner and thus can be representative of the whole batch.

STATISTICAL QUALITY CONTROL

- It is a technique for controlling quality of product using a set of statistical tools

- It involves two elements:

- Statistical process control: This summarizes collection of data , makes use of control charts.

- Acceptance sampling

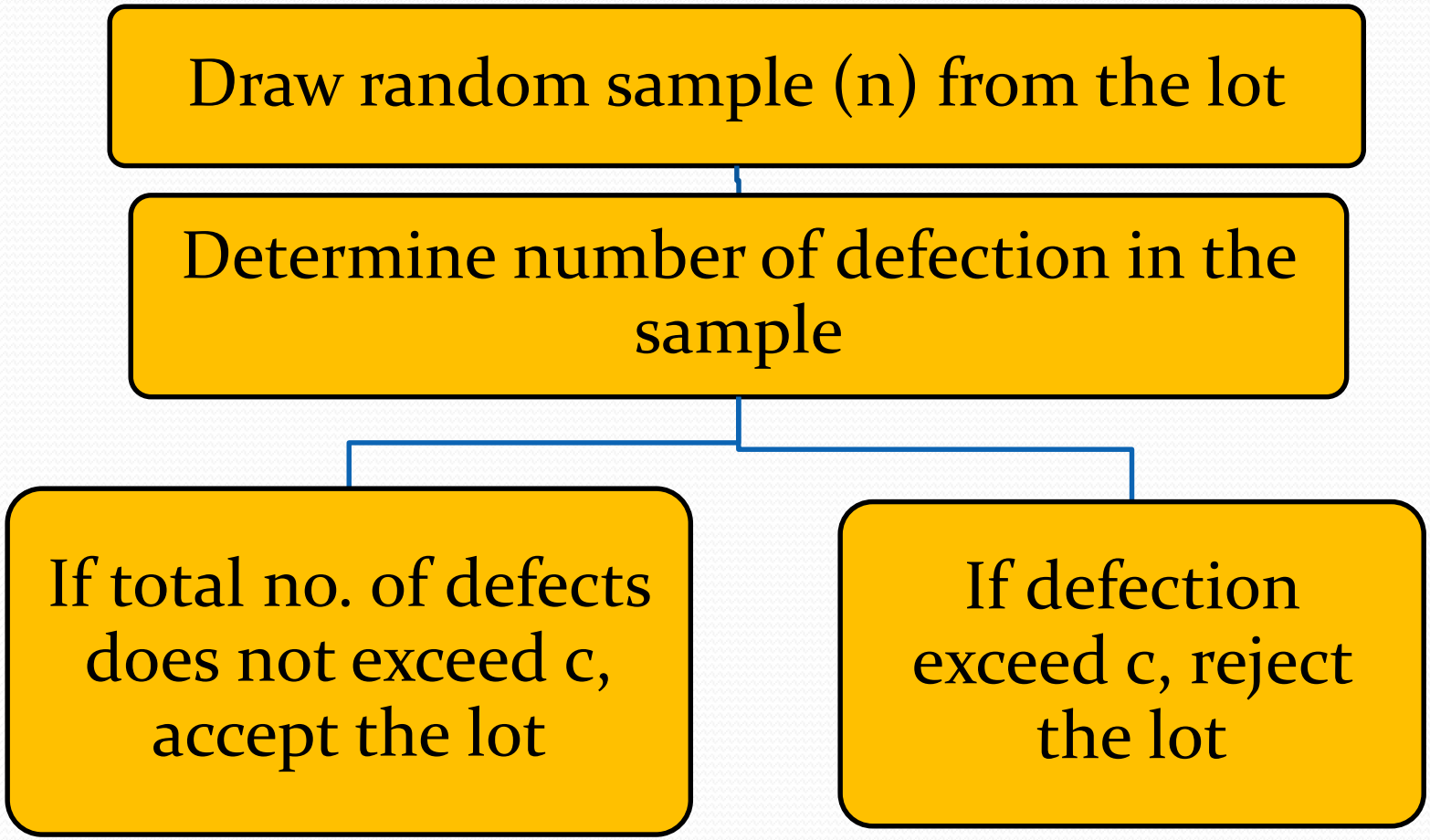
CONTROL CHARTS

- Primary purpose of control charts is to indicate when production processes might have changed sufficiently to affect product quality.
- If the indication is that product quality has deteriorated, corrective is taken.
- Compare attributes (No. of defectives in a sample)or variables (characteristics that can be measured on a continuous scale (weight, length, etc.) of the sample with that of the standard

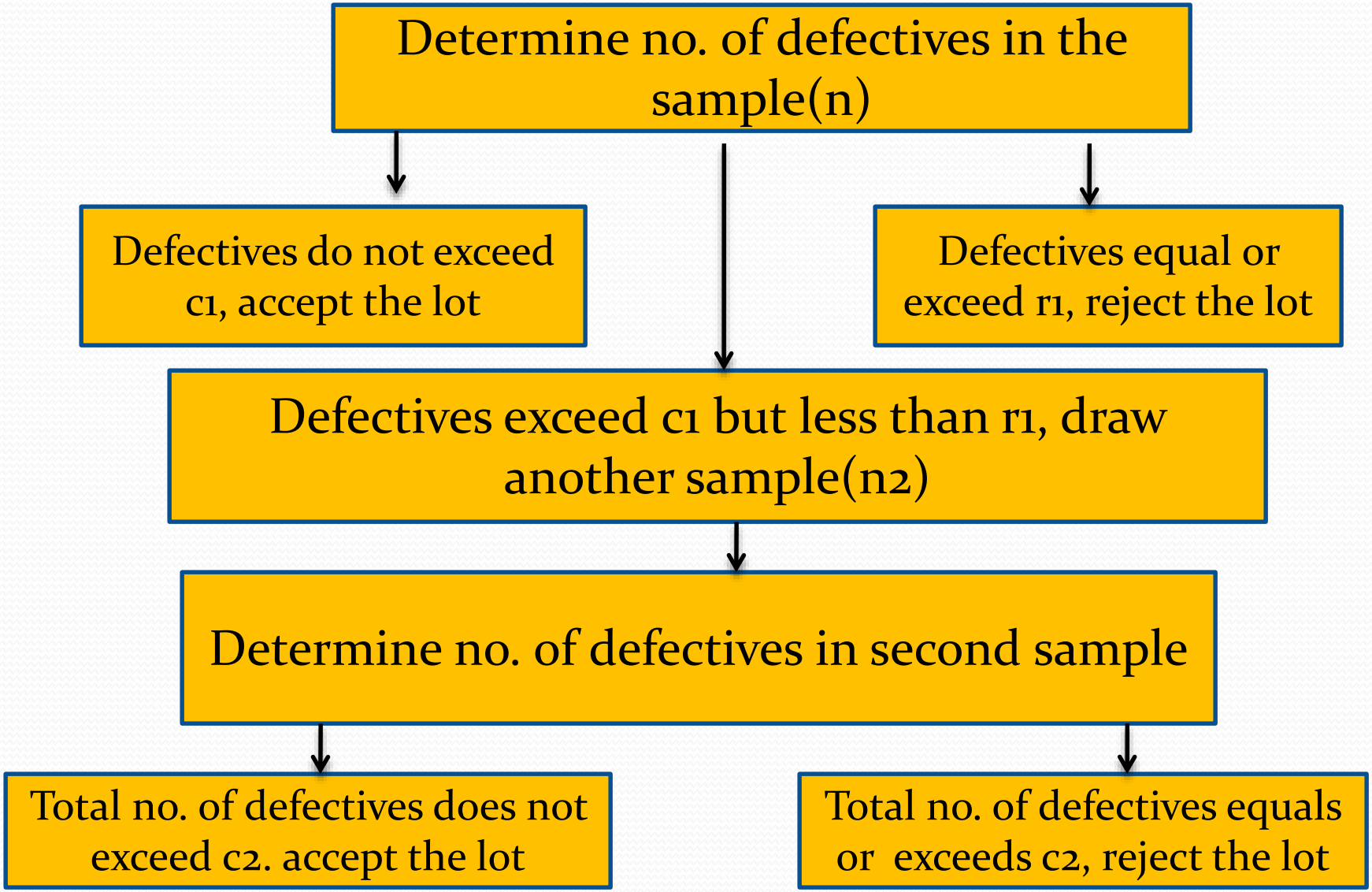
ACCEPTANCE SAMPLING OR SAMPLING INSPECTION

- It is the process of evaluating portion of the product material in a lot for the purpose of accepting or rejecting the lot as either conforming or not conforming to quality specifications.
- The acceptance plan identifies the:
  - Size of samples, n
  - Type of samples
  - Decision criterion, c, used to either accept or reject the lot
- Samples may be either single, double, or sequential.

SINGLE SAMPLING PLAN



DOUBLE SAMPLING PLAN



SEQUENTIAL/MULTIPLE SAMPLING

- This is extension of double sampling plan
- At each stage of sampling the cumulated results are analysed to take decision of accepting/rejecting the lot
- If no final decision can be taken at anyy stage, then another sample is drawn to take further decision.

QUALITY AUDIT

- ISO defines audit as systematic and independent examination to determine whether quality activities and related results comply with planned arrangements and whether these are implemented effectively and are suitable to achieve objectives.
- It checks if quality system and procedures are

✓ Free from congenital defects

✓ Are capable of achieving and maintaining standards of quality chosen by enterprise or costumers

✓ being adhered to and compiled with, in day to day work.

QUALITY AUDIT AND FOLLOW UP

- Prior to writing auditing report, auditor explains the observations to auditee
- Corrective actions to be taken are proposed
- Audit report are written in standard format which contain area audited, dates of audit, persons contacted, commendable features and recommendations.
- The report must contain status of implementation of pending corrective measures as per previous audit.

QC INSPECTION IN DISTRIBUTION AND STORAGE

GMP summarises following principles with respect to distribution:

- ✓ Only authorised products are distributed
- ✓ Premises are suitable for their intended use and kept on good sanitary condition
- ✓ All products are received, stored and handled carefully
- ✓ All operations are performed according to written procedure, supervised and documented
- ✓ Adequate provision exist to handle complaints, recalls and return goods

- Storage: Warehouse should be clean, inaccessible for unauthorised persons, temperature and humidity control, adequate shelving, free from insects and vermin.

- Special storage:

✓ Availability of cold room/refrigerator for vaccines and biological products

✓ Special storage areas for controlled drugs and other prescription drugs

✓ Suitable and secure storage facility for controlled drugs and poisons

CONCLUSION

- Quality is a never ending prospect.....
- Increase in quality, increases production, decreases cost and increases profits
- Thus quality control and inspection form an integral part of a company's management.

THANKYOU