ADITYA
PHARMACY COLLEGE

Documentation in Pharmaceutical industry - II

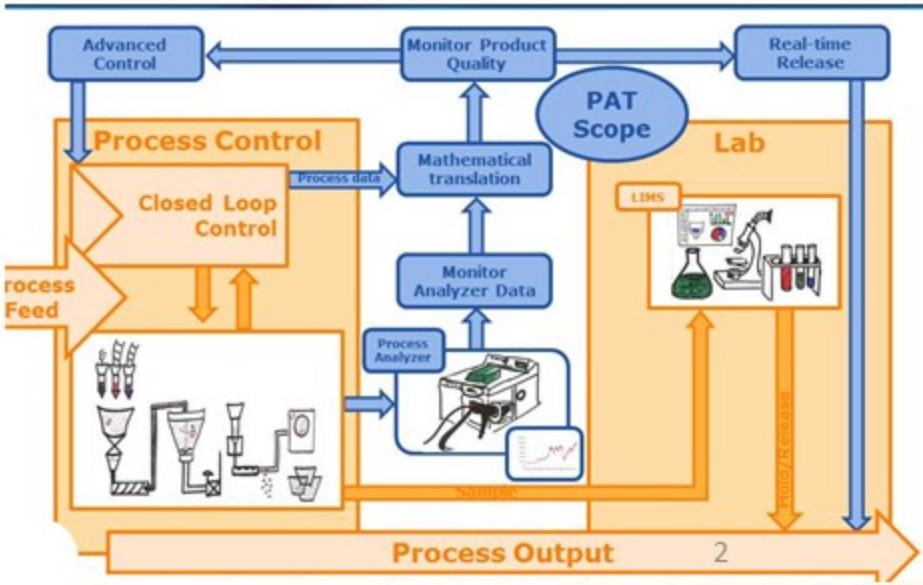
Dr. D. SathisKumar,

Professor,

Aditya Pharmacy College, Surampalem

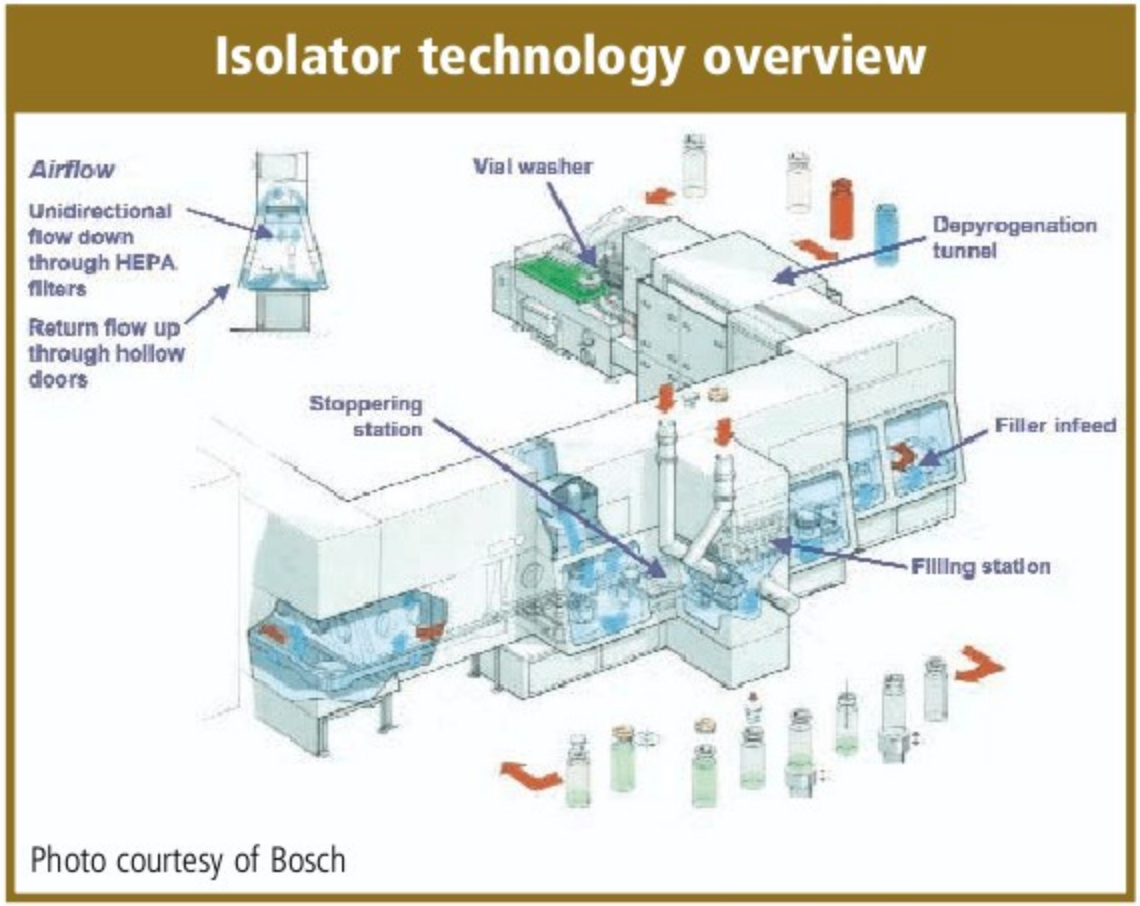
Specifications and Testing Procedures Specification

- A document describing in detail the requirements with which the product obtained during manufacture have to conform
  - Each specification should be approved and maintained by the quality control unit
  - Periodic revisions of the specifications may be necessary to comply with new editions of the national pharmacopoeia or other official pharma compendia
  - Testing procedures described in documents should be validated in context of available facilities and equipment before they are adopted for routine testing
- For starting and packaging materials
  - The designated name and internal code reference;
  - The reference, if any, to a pharmacopoeial monograph; and
  - Qualitative and quantitative requirements with acceptance limits
- For intermediate and bulk products
  - Specifications for intermediate and bulk products should be available if these are purchased or dispatched, or if data obtained from intermediate products are used in the evaluation of the finished product.



Testing procedures specification

- For finished products
  - The designated name of the product and the code reference where applicable
  - The designated names of the active ingredients
  - A description of the dosage form and package details
  - The qualitative and quantitative requirements with acceptance limits
  - The storage conditions and precautions, where applicable; and
  - The shelf- life.
- For containers and closures:
  - All containers and closures intended for use shall comply with the pharmacopeia requirements.
  - Suitable validated test methods.
  - Sample sizes, specifications, cleaning procedure and sterilization procedures, where ever indicated, should be followed strictly to ensure that these are not reactive, additive, and adsorptive or leach and neither effects the quality or purity of the drugs



Specifications:

- Describe the required characteristics or composition of a product or material or test, while test procedure is required to evaluate the specific quality attributes
- Provide the specific details defining the quality of:
  - Raw materials
  - Starting material
  - Packaging materials,
  - Intermediate and bulk products
  - Finished products.
- All specifications should be approved by authorised personnel (QC/QA manager)

Specifications : starting materials and packaging materials

- Description of the material
  - Designated name of material & internal code reference
  - Reference, if any, to pharmacopoeia monograph
  - Name of approved suppliers, and if possible, original producer of the products
  - Specimen of printed materials, including colour
  - Microbiological standards, if any;
- Where appropriate the content shall include for :
  - directions for sampling and testing or reference to procedures;
  - qualitative and quantitative requirements with acceptance limits;
  - storage conditions and precautions; and
  - the maximum period of storage before re-examination
  - Assurance for materials from animal parts origin should be free from undesirable disease (e.g. Transmissible Spongiform Encephalopathy).

Specifications for intermediate and bulk products

- shall be available if purchased or transferred or
- if data obtained from intermediate products are used for the evaluation of the finished product
- the specifications shall be similar to specifications for starting materials or for finished products

Specifications – finished products

- Designated name of product (and internal code reference where applicable);
- Formula or a reference to;
- Description of dosage form and package details;
- Directions for sampling and testing or reference to procedure where applicable;
- Qualitative and quantitative requirements with acceptable limits where applicable;
- Storage condition and any special handling precautions, where applicable;
- Shelf-life or expiry date.

Specifications – finished products

- Qualitative and quantitative requirements, with the acceptance limits, where applicable:
  - Physical appearance such as colour, taste, texture, size, etc;
  - Uniformity of weight (for tablets and capsules), disintegration (for tablets, capsules and pills), hardness and friability (for tablets), and viscosity (for internal and external liquids);
  - Heavy metals limits;
  - Microbial limits;
  - Other tests, as required, such as preservatives

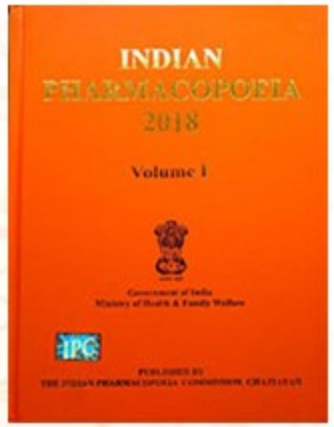
Procedures

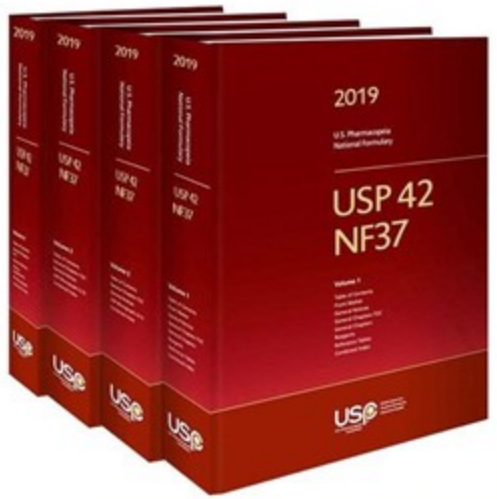
- The tactical document that outlines the activities or operations of the organisation in implementing the stated quality policies.
- Objectives :
  - Describe in detail how activities should be done, controlled and recorded in implementing the definite policy
- Standard Operating Procedures explains:
  - What the process is and it's purpose
  - Where activity is operating
  - Who is responsible for every activity
  - When activity is completed, sequential of the activities, frequency, etc.
  - How activity can be finished follow the work instruction design or other reference documents
  - Reference to the other relevant documents
- User :
  - All personnel who set up and run the processes

Decision-making using the Quality Policy

Testing Methods and Results

- Analytical methods and test procedures should be cross referenced (e.g. pharmacopoeia) or detailed to be understood by the local analyst.
- Formulae – with explanations and simplifications. This makes easy review by a second person





Out of Specification Results

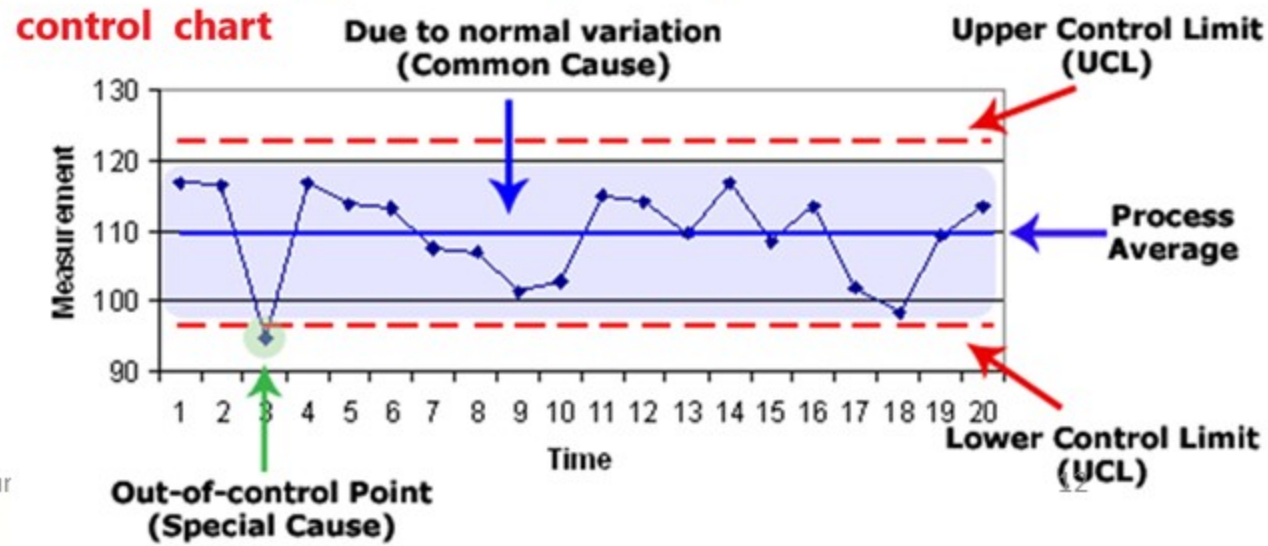
Must be handled based on a written procedure, that includes:

- Checklist of potential defects (e.g. calculations, methods, visual appearance, test procedure modified, experience of analyst during test, calibration of equipment …)
- Similar checklist for potential deviations in production
- Checking sampling and sampling devices
- Guidance on when re-sampling and re-testing may be required and documented justification in each instance
- Inclusion of known control sample in any testing

Approval and Rejection of Results

- Before approval or rejection – criteria to be used and results to be averaged should be specified in SOP(s)
- Criteria to include - averaging and/or rounding results and comparing results against specifications
- Control charts can be used to detect trends and atypical results
- Rounding results should be according to pharmacopoeial requirements (see also ICH Q3A)

NB: take care when averaging results from atypical values e.g. outliers, or single result out of specification limits



SUPPORTING DOCUMENTS OR WORK INSTRUCTIONS

- The operational document containing instructions specifying how the activities are performed or products are accepted.
- SOP and work instructions can be merged depending on the documentation system adopted by the company.
- Objectives :
  - It is an instruction document, step by step for guideline to execute the daily activity or operation for personnel in every function
  - It is used departmentally, every task or every line.
- Content of work instructions :
  - Detailed explanation of instructions to finish the job, detailed handling of method, equipment and machine
  - Related to the technical matters with stressing for operation, inspection & testing.
- User :
  - All personnel who operates the certain task
- Supporting documents:
  - Worksheet, checklist
  - Visual (illustration, flow chart, layout plan, photo)

Quality Procedure/SOP

- Process oriented
- Describe step of procedure
- Supporting the Quality Manual
- Explain general description on certain process and give systematic action to ensure product quality
- Procedure guideline which involve several departments and/or sections
- During implementation need other supported documents
- Guideline at organization level

Working Instruction

- Task oriented
- Describe detail instruction
- Operation guidance
- Dedicated to explain special task, method, or technique which should be done to achieve target quality
- Instruction guidance which dedicated for certain department or section only
- During implementation can stand alone
- Guidance at operational level

Records

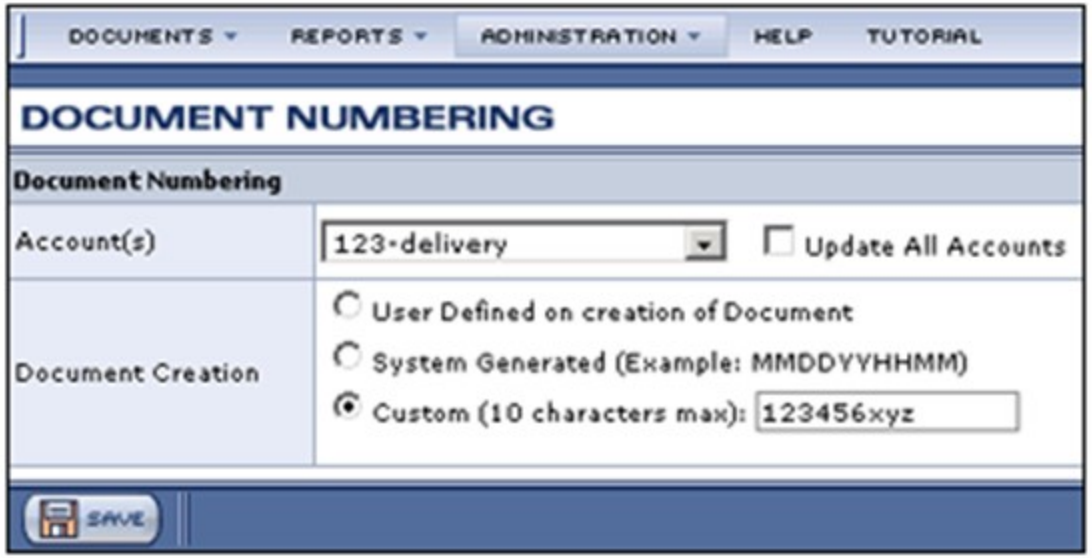
- Records, including charts and data pertaining to design, inspection, testing, survey, audit, review or related results, should be maintained as important evidence to demonstrate:
- Quality System has been effectively implemented;
- that products and services have been developed and delivered appropriately with the requirements.
- All Records should be :
  - legible and clear;
  - Dated;
  - readily identifiable and retrievable;
  - carry authorisation status;
  - retained for a designated period;
  - protected from damage and deterioration while storage.
  - All calculations should be duly recorded

Format of document

- No “best format” in documentation system.
- Each document should be suitable for all users
- In general, all quality documents can be written in the following format :
  - narrative
  - flowchart
  - combination narrative and flowchart
  - electronic / computerized system

Document numbering system

- Every document shall have a unique number
  - to facilitate traceability
  - Yet simple to facilitate saving and controlling of the document



Content of document

What should be written in the document:

- Name of document
- Name of company, department or division of the maker
- Document number
- Revision number
- Page and number of pages of document
- Date of approved
- Effective date
- Name and signature of the person who prepared the document
- Names and signatures of the person who reviewed and person approved the document
- Content of procedure/instruction

Narratives document

- The most common format being used
- The narrative document can be described as the following:
  - Policy reference
  - Objective : why and for what
  - Coverage area
  - Document reference
  - Responsible person
  - Detail procedure
  - Record if needed

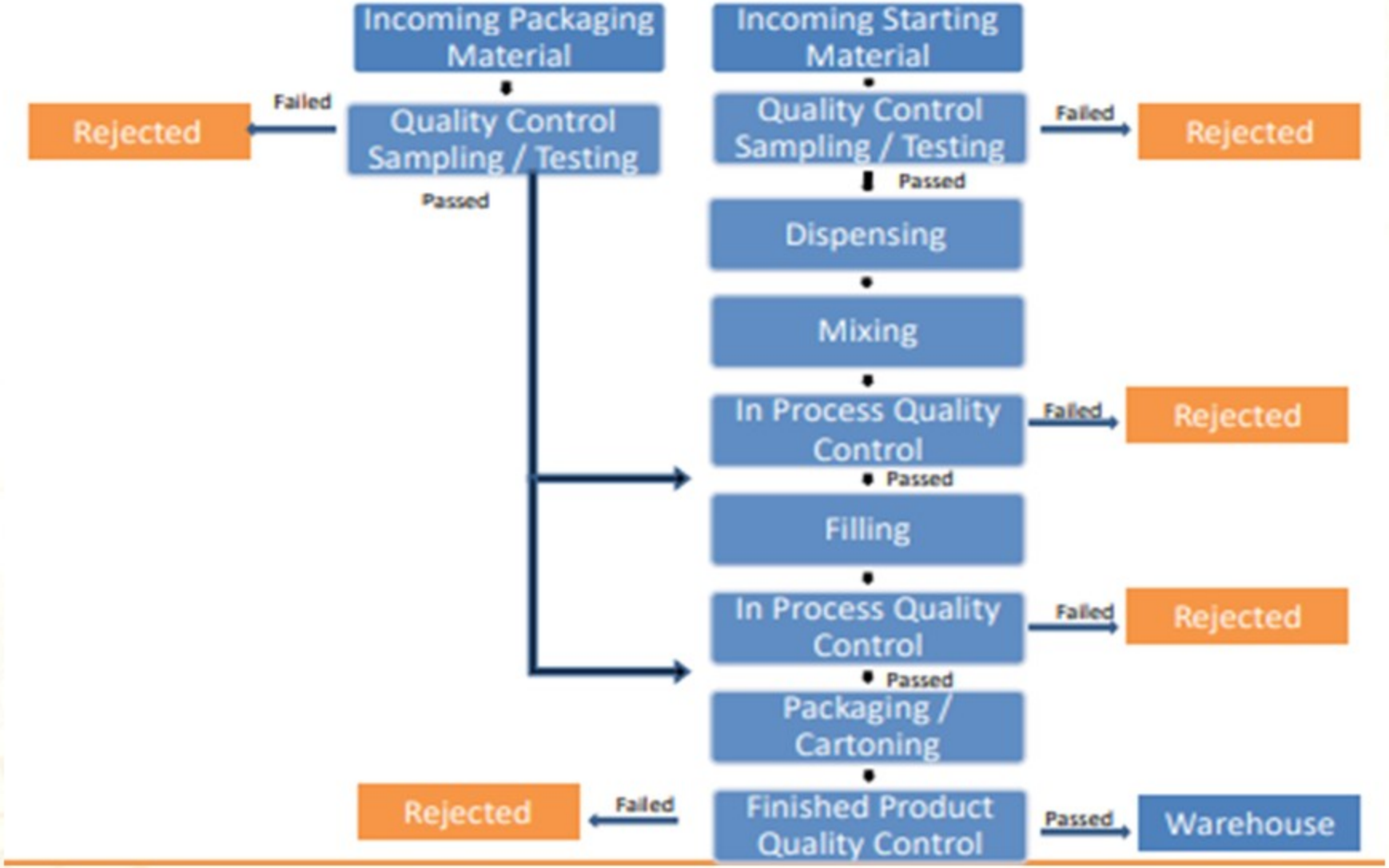
Flow chart document

- Schematic representation which describe the flow of processes in certain target activity
- Very clear and easy to understand
- Sample of the flowchart document can be written as beside schema
- For complicated process, sometimes flowchart alone might not be able to capture detailed information therefore it should be combined with a narrative

Flow chart document

Flow Chart 3 : Production of Bulk Item

Typical Production flowchart

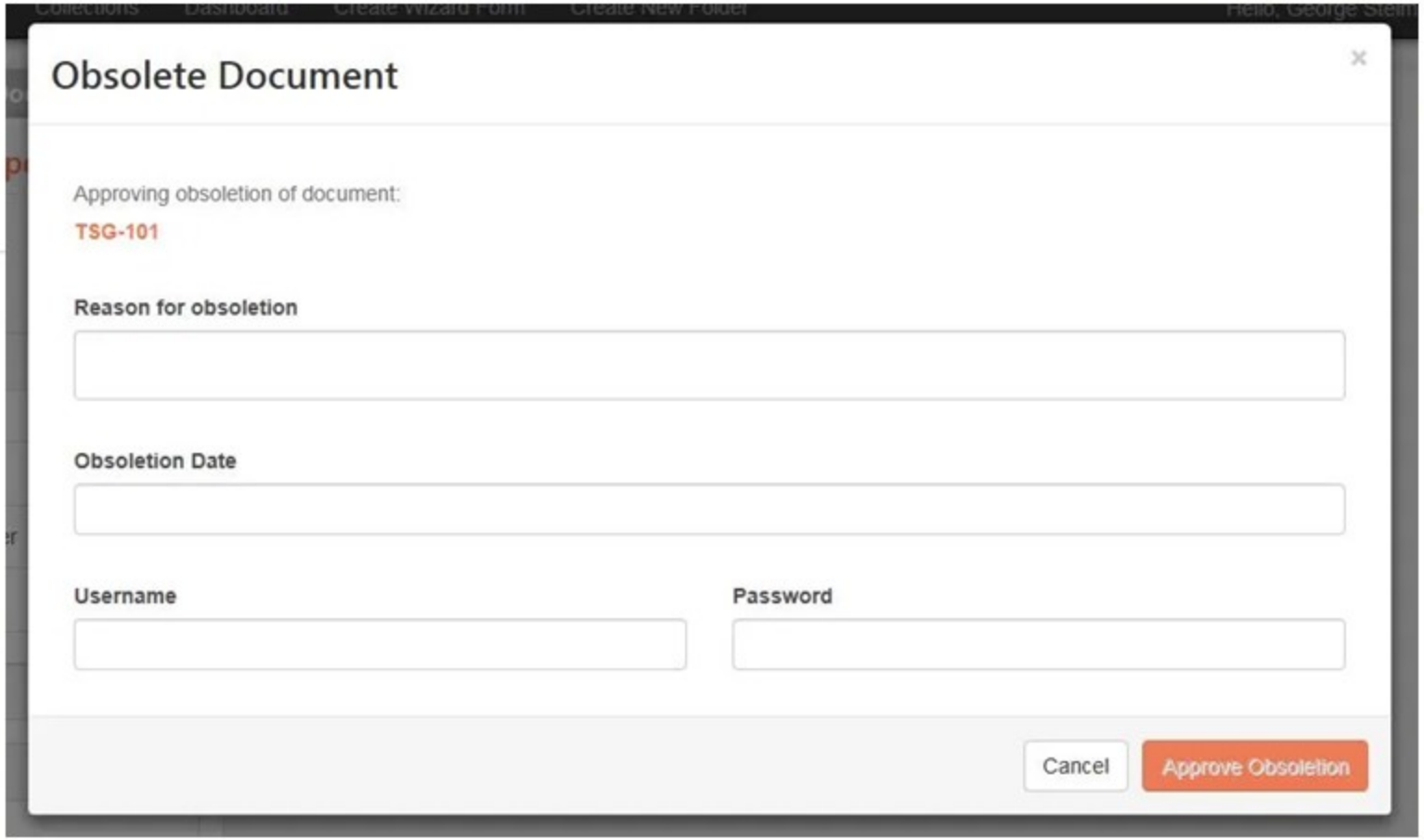


Document control

As mentioned in the previous slides, documents shall:

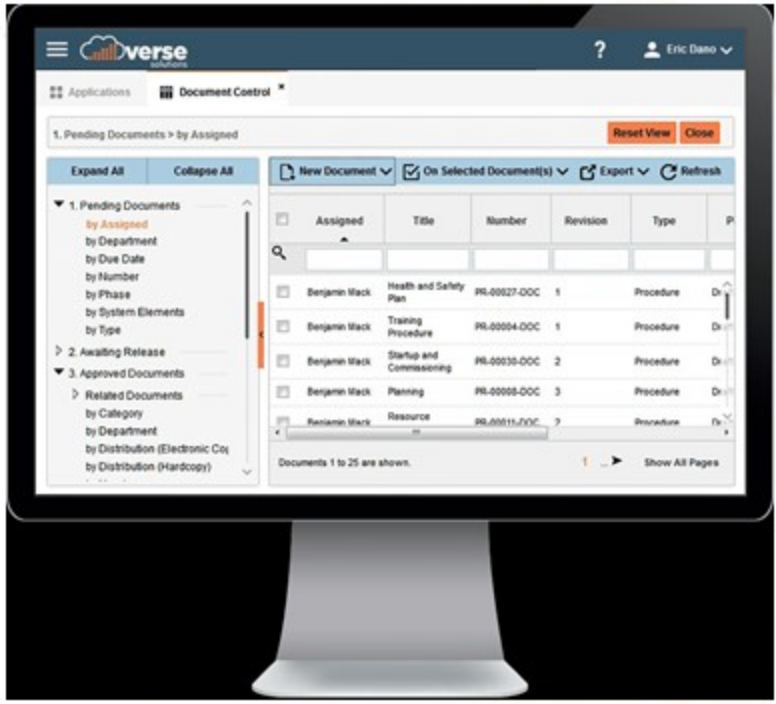
- Be approved, signed and dated by appropriate authorised persons
- Be properly authorized before making any change
- Records shall be made or completed each time action is taken in such a way that all significant activities concerning the manufacture of the product are traceable
- There shall also be a way to differentiate master hard copy document from all duplicated copies (e.g. stamp "MASTER WHEN RED" on master copy and stamp "CONTROLLED COPY" on distributed copies)
- Distributed documents should be recorded (e.g. using distribution list)
- Obsolete documents:
  - Control copies shall be retrieved from users based on distribution list and properly destroyed to prevent inadvertent use
  - Obsolete master documents shall be marked "obsolete" and archived
- Create a list/index of all documents established.

Obsolete document



Distribution of documents

- Only up-to-date documents shall be distributed
- Copy of documents should be distributed to relevant parties and available at point of use e.g. Processing and Packaging Instructions should be available in Production Areas whereas Test Methods shall be available in QC labs
- Only document Controller or QC/QA are authorised to distribute the document in accordance to written procedure



REVIEW AND REVISION OF DOCUMENTS

- Documents shall be reviewed periodically to confirm that they are up to date.
- Changes to the procedures/steps on the document shall go through the proper change control and approved by an authorised person
- The newly revised documents shall state:
  - The date of revision
  - Reason for the revision
  - The new effective date

RECORD KEEPING RULES “Do Not” Rules

- DO NOT leave any blanks in forms (shall indicate “nil” or “N/A” when there is no legitimate entry)
- DO NOT leave mistakes uncorrected (check your entries)
- DO NOT scribble out mistakes (shall not obscure original entries)
- DO NOT write correct entries over incorrect entries (writing over shall not obscure original entries)
- DO NOT forget to initial and date entry
- DO NOT use pencil (all entries should be made using permanent ink)

List of documents required

- Quality Control Documents
- Production Documents
- Standard Operating Procedures (SOPs) and Records

Production documents

- Manufacturing Formula and Processing Instructions
- Packaging Instructions
- Batch Processing Records
- Batch Packaging Records

Continue ……