GMP training
for Cosmetic products GMP based upon the principles of ISO22716

A Two Day training by SGS
Dubai, 19 – 20 Nov. 2013

by:
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WHEN YOU NEED TO BE SURE SGS

Introduction

- **Intesar Ahmed Khan**
- B.Sc (Hon), Dairy Tech
- Technical Manager
- Lead Auditor & Trainer
- HACCP / QMS / FSMS /SQF/ BRC / GMP
- SGS Gulf Ltd
- Middle East Regional HQ
- Jebel Ali Free Zone
- DUBAI (UAE)

Basic Principles of GMP and quality assurance

Section 1 – 'Course introduction' and 'General principles of GMP and quality assurance'

WHEN YOU NEED TO BE SURE SGS

GMP introduction
Objective for this session …

- To equip participants with a basic knowledge of GMP
- To understand key issues in quality assurance / quality control
- To understand specific requirements on organization, procedures, processes and resources.

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Introduction to Cosmetics GMP

WHEN YOU NEED TO BE SURE

GMP - Good Manufacturing Practice

- Require a quality approach to manufacturing, enabling organisations to minimise or eliminate incidents of contamination, mix-ups and errors;
  - starting with the purchase & receipt of qualified raw materials and supplies which after verification are released to production, and
  - ending with the review, release, and shipment of the finished product to assure that it complies with the stated requirements.

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GMP in the Cosmetics Supply Chain

- "CRITICAL" processes = Everything that directly or indirectly may have a (negative) impact on quality of the product;
  - ' quality ', related to the safety to consumers
  - ' critical ' versus ' non-critical ': risk assessment
    - ISO 29621:2010; Cosmetics — Microbiology — Guidelines for the risk assessment and identification of microbiologically low-risk products

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GMP in the Cosmetics Supply Chain

Three main elements to control quality:

- Identity,
- Quantity, and
- Purity, of cosmetic products.

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GMP ... avoidance of:

- Mix ups
  - For example, to prevent the mix up of lables during a labeling and packaging operation.
- Contamination
  - For example, to avoid the microbiological contamination in high-risk products, like in shampoo.
- Cross-contamination
  - For example, to avoid spilling product A lot 1 into the next batch of the same product A, lot 2.

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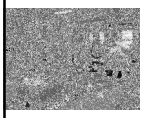
GMP.....Where to apply?



- Blend vessel; GMP required?
  - ??
- Parking area; GMP required?
  - ??
- Offices; GMP required?
  - Depending on situation!
  - Purchasing?
    - Vendor qualifications: ??
  - HR?
    - Training: ??
    - Personnel contracts: ??
  - Finance?
    - ??

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Does GMP cover everything?

No!

- Not safety aspects for manufacturing personnel
- Not aspects of protection of the environment (national laws).

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Regulatory status in relation to Cosmetics GMP

WHEN YOU NEED TO BE SURE

Regulatory Product Types

Table 1: Illustrative Examples of Product Categorisation in Different Markets				
Product Type[1]	**Market**			
	EU	**USA**	**Japan**	**Canada**
Soap for hands	Cosmetic	Cosmetic	Cosmetic	Cosmetic
Lipstick	Cosmetic	Cosmetic	Cosmetic	Cosmetic
Sunscreen	Cosmetic (subject to positive list)	Over-the-counter (OTC) drug	Cosmetic	Non-prescription drug
Anti-acne lotion	Medicinal product	OTC drug	Quasi-drug	Non-prescription drug
Anti-caries toothpaste	Cosmetic	OTC drug	Quasi-drug	Non-prescription drug
Anti-perspirant	Cosmetic	OTC drug	Quasi-drug	Non-prescription drug
Hair dye	Cosmetic	Cosmetic	Quasi-drug	Cosmetic

[1] The types of products referred to in this table are 'normal' products, i.e. products not having the composition or claims more appropriate for another product category. For example, in the case of lipstick, the product considered is a lipstick having no additional SPF function.

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Regulatory ref. ISO 22716

WHEN YOU NEED TO BE SURE

ISO 22716

ISO = International Standards Organisation comprising 157 member countries → therefore wide acceptance.

ISO 22716: 2007 – published 15 NOV 2007

Other guidance and technical documents published by TC 217 to support developing a GMP structure in cosmetic organizations.

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ISO 22716 status

- International Cooperation on Cosmetic Regulation (ICCR; US, EU, CA, JP), annual meetings AUG 2008 and SEP 2009:

The Regulators agreed to implement ISO Standard 22716 in their respective regions, wherever possible. Regulators summarized the situation in their respective regions, as follows:

- US: agreed to take into consideration ISO International Standard 22716 and modify current FDA guidance.
- EU: will implement ISO TC-217 International Standard 22716 adopted by CEN.
- Canada: agreed to take into consideration ISO International Standard 22716 and expects to adopt voluntary GMP standards by ICCR-3.
- Japan: notified local governments that JCIA adopted ISO International Standard 22716.

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ISO 22716 GMP

- Not covered by ISO 22716 (not exclusive listing):
  - Detailed description of classes of products
  - Detailed description of parameters (f.e. clean room conditions)
  - Distribution
  - Risk Assessment process
  - Qualification and validation: Master Plan, Process validation, etc.
  - GMP for ingredients

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Some words on Quality Management

WHEN YOU NEED TO BE SURE

Quality Management

Quality Management

- Determines and implements the “quality policy”
- The basic elements are:
  - An appropriate infrastruture or “quality system” encompassing the Procedures, Processes, and Resources
  - The systematic actions necessary to ensure adequate confidence that a product (or service) will satisfy given requirements for “Quality”

The totality of these actions is termed “Quality Assurance” or better use: “Quality Management”

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Quality Management

Quality Management

- Terminology may differ
  - “Quality System” is said to be rarely used in GMP
- The concepts of QA, GMP and Quality Control are interrelated aspects of Quality Management.
  - They are described on the following slides in order to emphasize their relationship and their fundamental importance to the production and control.

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Implementing ISO 22716

- **Independency of the quality unit (3.2.1.3).**
  - The quality unit needs to be independent in its decision making process from the Manufacturing or Operations unit. This can be found in the Organizational charts: both the Quality unit and the Manufacturing or Operations units need to report to the senior management of the site. The Org chart needs to be a unique (version controlled) document and signed & dated by the senior management. Individual job descriptions of the head of quality and the head of manufacturing need to be published and also signed by their resp. managers. The job description of the head of quality needs to contain clear references to the responsibilities and authority of quality issues: to release product, move product to a different status (e.g. quarantine, release, rejected), deviation control and investigation, change control, internal audit, etc.

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Quality Management

Principles of Quality Management

- Wide-ranging concept
  - Covers all matters that individually or collectively influence the quality of a product
- Totality of the arrangements
  - To ensure that the product is of the right quality for the intended use
- Quality Assurance incorporates GMP
  - product design and developments which is outside the scope of this module

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Quality Management

Requirements for QA Systems – I

1. Ensure products are developed correctly
2. Identify managerial resposibilities
3. Provide SOPs for production and control
4. Organize supply and use of correct starting materials
5. Define controls for all stages of manufacturing and packaging

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Quality Management

Requirements for QA Systems – II

6. Ensure finished product correctly processed and checked before release
7. Ensure products are released after review by authorized person
8. Provide storage and distribution
9. Organize self-inspection

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Quality Management

GMP

- Ensure that products are consistently produced and controlled
- Diminishes risks that cannot be controlled by testing of product
  - Cross-contamination
  - Mix-ups

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Quality Management

Basic Requirements for GMP – I

1. Clearly defined and systematically reviewed processes
2. Critical steps validated
3. Appropriate resources: personnel, buildings, equipment, materials
4. Clearly written procedures
5. Trained operators

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Quality Management

Basic Requirements for GMP – II

6. Complete records, failure investigations
7. Proper storage and distribution
8. Recall system
9. Complaint handling

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Quality Management

Quality Relationships

Quality Management

⇩

Quality Assurance

⇩

GMP

⇩

Quality Control and Manufacturing

GMP (Good Manufacturing Practice) for Cosmetic Products

End of Section 1

WHEN YOU NEED TO BE SURE SGS

GMP (Good Manufacturing Practice) for Cosmetic Products

Section 2: Personnel; training; Sanitization & cleaning

WHEN YOU NEED TO BE SURE SGS

GMP Section 2 - Outline

With reference to ISO 22716 as basis:

- Organization & Personnel
- Sanitization
- Cleaning

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Organization & Personnel

Organization

- First document required by ISO 22716 = Organization Chart!

The Org Chart must:

- Define the organizational structure → understandable organization and functioning of the staff
- Be appropriate for the size of the company
- Be appropriate for the diversity of its products
- Show independence! (see next slide)

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Organization & Personnel

Organization

- Ensure adequate staffing levels in all scopes of activity
- The functioning of the staff of the company be understandable – Job Description*
- Personnel are adequately trained to perform their activities covered by GMP.

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Organization & Personnel

Organization – Management Responsibilities

ISO 22716:

- Top management to support organization
- Top management implements GMP with participation & commitment of personnel in all departments and at all levels
- Top management defines and communicates the areas in which authorized personnel are allowed to access

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Organization & Personnel

Organization – Management Responsibilities

There should be:

- Organization Chart
- Job Descriptions of all personnel
- Training Records of all personnel

And review these regularly!

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Organization & Personnel

Organization – Personnel Responsibilities

ISO requires all personnel should:

- Know their position in the organizational structure
- Know their defined responsibilities and activities
- Have access to and comply with documents relevant to their particular responsibility scope
- Comply with personal hygiene requirements
- Be encouraged to report irregularities or other non-conformities which may occur at the level of their responsibilities
- Have adequate education training and skills to perform the assigned responsibilities and activities

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Organization & Personnel

ABC Cosmetic Factory Ltd.

Standard Operating Procedure	Section : 01 Organization and Personnel	SOP No. : 1.2
	Title : Management Responsibility	Revision No. : 00
Date Issued: 30.12.97		Effective Date: 02.01.98
		Supersedes : N/A
Prepared by :	Approved by :	Page 1 of 4

1.0 Purpose
To outline the basic responsibilities of key personnel of the plant.

2.0 Scope
This SOP applies to all key personnel in the plant addressed below.

3.0 Responsibility
It is the responsibility of the Plant Manager to define the responsibilities of the key personnel, to ensure that this SOP is updated accordingly with changes in their responsibilities, and to clearly relay these responsibilities and job duties to these personnel. It is the responsibility of the key personnel addressed in this SOP to adhere to and perform their functions and report to the Plant Manager as necessary.

4.0 Basic Responsibilities

4.1 Plant Manager
4.1.1 To ensure that adequate resources are being effectively distributed in each single operation.
4.1.2 Supervise and provide technical supports to quality control, production and administration functions.
4.1.3 Responsible to review and approve all production and process related documents and SOPs.
4.1.4 Ultimate responsible of the quality system of the plant.
4.1.5 To ensure that good manufacturing and safety practices are being exercised and implemented in the plant.
4.1.6 Responsible to maintain all staff qualification records and identify the training needs for key personnel.
4.1.7 Responsible to review the quality system at defined intervals sufficient to ensure its continuing suitability and effectiveness.
4.1.8 Prompt the QC functions, for initiating any investigation and measures.

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Organization & Personnel

Personnel – Principle

"*… should have skills based on relevant training and experience acquired, or any combination thereof, that are appropriate to their responsibilities and activities.*"

ISO 22716:2007 – 3.4.1

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Organization & Personnel

Personnel – Principle

"*… should have skills based on relevant training and experience acquired, or any combination thereof, that are appropriate to their responsibilities and activities.*"

Experience – you can define this in the "position requirement".

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Organization & Personnel

Personnel – Experience

Qualification – Examples

- Chemistry, biochemistry, chemical engineering, microbiology, pharmaceutical sciences and technology, pharmacology and toxicology, physiology; or
- Other related science or GMP-related subjects relevant to the responsibilities to be undertaken

Practical Experience – Examples

- Under professional guidance
- Resolve the problems encountered in manufacturing and QC

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Organization & Personnel

Personnel – Principle

"*… should have skills based on relevant training and experience acquired, or any combination thereof, that are appropriate to their responsibilities and activities.*"

Training requirements are as follows…

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Implementing ISO 22716

- **Training (3.4.2.3), and re-training (3.4.2.5).**
  - The training program should contain both initial training for new personnel joining the organization, and also continued (e.g. annual) re-training for personnel and also training to put in place after changing certain types of operations or procedures. Training is a continuous effort for Cosmetics manufacturers. It needs to be documented: a written program adopted and signed off by senior management; records for each individual attending training; listing containing signatures of employees who did follow a given course on given dates; certificates (signed and dated) to be obtained after successfully doing an exam following the training.

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Training under ISO 22716


TECHNICAL REPORT

ISO/TR 24475

First edition
2010-03-01

Cosmetics — Good Manufacturing Practices — General training document

Cosmétiques — Bonnes pratiques de fabrication — Document général de formation

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Organization & Personnel

Organization – Personnel Training

ISO 22716's definite requirement:

- GMP training --- provided for all personnel! (Induction+)
- Training programme – identifies training needs of ALL personnel
- Training courses – tailored to individuals (considering their expertise and experience, jobs and responsibilities)
- Training – in-house or external expert organizations = acceptable
- Training – should be constant and ongoing

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Organization & Personnel

Organization – Personnel Training

Key points:

- TRAINING PROGRAMME
- TRAINING RECORDS

For which – GMP training included for everyone!

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Organization & Personnel

Organization – Personnel Training

How do you evaluate the effectiveness?

"*Knowledge accumulated by personnel should be evaluated during and/or after training.*"

ISO 22716:2007 – 3.4.4

Basic Principles of GMP

Sanitation and Hygiene

Section 2 – Personnel; training; sanitization & cleaning

WHEN YOU NEED TO BE SURE

Organization & Personnel

Personnel Hygiene & Health

Hygiene Programme

"…should be established and adapted to the needs of the plant. These requirements should be understood and followed by every person whose activities take them into production, control and storage areas."

ISO 22716:2007 – 3.5.1.1

Organization & Personnel

Personnel Hygiene & Health

ISO requires that:

- Personnel to be instructed to use hand washing facilities
- Every person entering production, control and storage areas to wear appropriate clothing and protective garments to avoid contamination of cosmetic products
- Eating, drinking, chewing, smoking or the storage of food, drink or smoking materials or personal medication in the production, control and storage areas to be avoided
- Any unhygienic practice within the production, control and storage areas or in any other area where the product might be adversely affected to be forbidden.

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Organization & Personnel

Personnel Hygiene & Health

ISO requires that:

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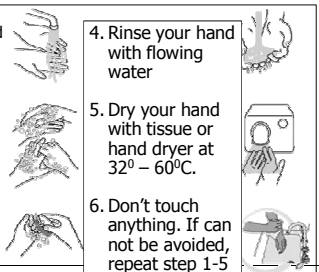
Organization & Personnel

Personnel Hygiene & Health

Tips – Hand washing guidance

1. Wet your hand with flowing water
2. Use soap around your hand and fingers.
3. If needed use brush to clean your nails



4. Rinse your hand with flowing water
5. Dry your hand with tissue or hand dryer at $32^0 – 60^0$C.
6. Don't touch anything. If can not be avoided, repeat step 1-5

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Organization & Personnel

Personnel Hygiene & Health

ISO requires that:

- Personnel to be instructed to use hand washing facilities
- Every person entering production, control and storage areas to wear appropriate clothing and protective garments to avoid contamination of cosmetic products
- Eating, drinking, chewing, smoking or the storage of food,

Meaning:
Clothing specifications for these areas to be defined

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Organization & Personnel

Personnel Hygiene & Health

Tips – Headwear, Bodywear, Footwear






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Organization & Personnel

Personnel Hygiene & Health

Meaning:
Specify these in your Hygiene Programme
Include these in your training
Assess adherence through monitoring

to avoid contamination of cosmetic products

- Eating, drinking, chewing, smoking or the storage of food, drink or smoking materials or personal medication in the production, control and storage areas to be avoided
- Any unhygienic practice within the production, control and storage areas or in any other area where the product might be adversely affected to be forbidden.

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Organization & Personnel

Personnel Hygiene & Health

Health

"Steps should be taken to ensure, as far as is practicable, that any person affected by an apparent illness or having open lesions on the exposed body surface should be excluded from direct contact with product until condition is corrected or determined by medical personnel that the quality of cosmetic products will not be compromised."

ISO 22716:2007 – 3.5.2

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Organization & Personnel

Personnel Hygiene & Health

Visitor or Untrained Personnel

- Given information in advance, in particular
  - Personal hygiene
  - Prescribed protective clothing
- Must be accompanied and closely supervised at all times

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Organization & Personnel

Personnel Hygiene & Health

Tips

- Personnel to undergo health examination.
- Encourage good personal hygiene e.g. regular bathing, teeth brushing, hand washing before enter production, after toilet, after eating, after smoking
- When designing processes – avoid direct contact of operators' hands and products

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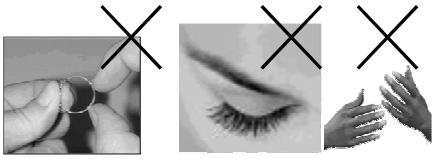
Organization & Personnel

Personnel Hygiene & Health

More Tips



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Sanitation and Hygiene

Objectives

- Review measures to ensure good sanitation in:
  - Premises
  - Equipment
  - Processes
- To review measures to ensure good personnel hygiene

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Sanitation and Hygiene

Scope

All aspects of manufacturing

- Personnel
- Premises
- Equipment
- Apparatus
- Production materials and container
- Products for cleaning and disinfection
- All potential sources of cross-contamination

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Sanitation and Hygiene

Design of Premises

- Design
  - *Walls, floors, ceilings, ledges, drains, air supply, dust extraction*
- Prevention of build-up of dirt and dust to avoid unnecessary risks of contamination
  - *Cleaning program, appropriate cleaning, cleaning records*
- Effective cleaning and disinfection
  - *Choice of materials and chemicals, validation*
- Drains
- Protection from insects, vermin and weather
  - *From receipt of raw materials to despatch of released product*

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Sanitation and Hygiene

Avoidance of (Cross-)Contamination I

- Segregated areas
- Ventilation systems and airlocks
- Clothing
- Closed processing systems
- Cleaning and decontamination

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Sanitation and Hygiene

Avoidance of (Cross-)Contamination II

- Ventilation systems and airlocks
  - Design of ventilation system
  - Incoming air should be filtered
  - Pressure differentials and air extraction
  - Airlocks
  - Airflow patterns and equiment design
  - Recirculation vs 100% fresh air supply

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Sanitation and Hygiene

Avoidance of (Cross-)Contamination III

- Clothing
  - Protection of operator and product
  - Highly potent products or those of particular risk – need for special protective clothing
  - Personnel should not move between areas producing different products
  - Garments need to be cleaned

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Sanitation and Hygiene

Avoidance of (Cross-)Contamination IV

- Closed processing systems:
  - For example: totally enclosed water purification systems
  - Tanks fitted with appropriate filtration – without removable lids
  - Present special cleaning difficulties, sometimes use clean-in-place (CIP)

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Sanitation and Hygiene

Avoidance of (Cross-)Contamination V

- Cleaning and decontamination
  - Procedure for removing soil and dirt
  - Remove all cleaning chemical residues or disinfectant residues
  - Must remove or reduce micro-organisms

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Implementing ISO 22716

- **Effectiveness of cleaning & sanitization (4.10.3).**
  - Under Cosmetics GMP following ISO22716 the formal validation of cleaning and sanitization procedures is not required. What the company has to do, though, is a formal assessment as to the usage and usefulness of such methods. So, sanitization method aiming to remove most of the microbial burden in the facility, in that case the company should have a purchasing program in place to order an appropriate disinfecting cleaning agent, as proposed by literature examples, eg. Here again a proper risk assessment based approach is the key and should be present.

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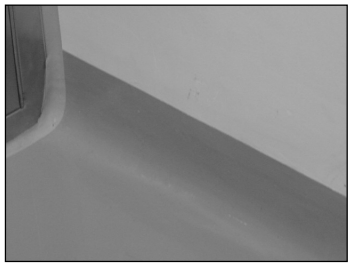
Construction of premises

- Walls



High density, smooth plaster, waterproofed by painting acrylic / high polymer enamel

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Construction of premises

- Ceilings

Light fittings without joint!

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Construction of premises

- Windows – should be non-opening!

All to allow for easy cleaning and sanitation!

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Sanitation and Hygiene

Production Operations – Sanitation – I

- Work-flow
  - Designed to avoid potential contamination
- Access
  - To production areas restricted to authorised personnel
  - Direct operators, QC staff, warehouse staff, maintenance personnel, cleaners
  - The more critical the area – fewer number of persons there

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Sanitation and Hygiene

Production Operations – Sanitation – II

Simultaneous operations

- Not permissible to process different products in different areas with a common ventilation system
- Permissible to carry out secondary packaging activities for different products within a packing hall with adequate physical separation

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Sanitation and Hygiene

Production Operations – Sanitation – III

Area clearance checks

- Process of checking
  - All materials and documentation from the previous batch removed
  - All plant and equipment thoroughly cleaned and appropriate status labelling
  - Checklist useful

Sanitation and Hygiene

Production Operations – Sanitation – IV

Area clearance checks

- The area clearance check should be carried out by two people preferably
  - Between batches of same product, acceptable for both checks to be carried out by production personnel
  - For product changeover, second check carried out by QC staff
  - All checks carried out in accordance with written SOP and results recorded on the batch documentation

GMP (Good Manufacturing Practice) for Cosmetic Products

End of Section 2

GMP (Good Manufacturing Practice) for Cosmetic Products

Section 3; Premises & Equipment; Qualification & calibration

WHEN YOU NEED TO BE SURE SGS

GMP Section 3 - Outline

With reference to ISO 22716 as basis:

- Premises & Equipment
- Qualification & calibration

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Premises

Principle

Located, designed, constructed and utilized so as:

- To ensure protection of the product
- To permit efficient cleaning, if necessary, sanitizing and maintenance
- To minimize the risk of mix-up of products, raw materials and packaging materials

All depends on the type of cosmetic product, existing conditions, cleaning / sanitizing measures used.

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GMP (Good Manufacturing Practice) for Cosmetic Products

Section 4: documentation & record keeping; Materials Management

WHEN YOU NEED TO BE SURE SGS

GMP Section 4 - Outline

With reference to ISO 22716 as basis:

- Documentation & record keeping
- Materials Management

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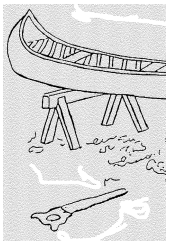
Documentation

What is being made?

Most of us when attempting a task need some sort of documentation



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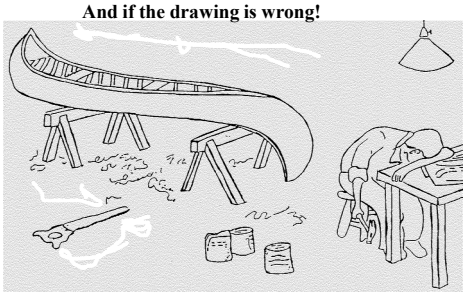
Documentation

And if the drawing is wrong!



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Documentation

Objectives

1. To review general requirements for documents
2. To review specific requirements for each document
3. To consider current issues applicable to specific situation

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Documentation - Purpose

"*Each company should establish, design, install and maintain its own system of documentation that is appropriate to its organizational structure and to the type of products*."

ISO 22716:2007 – 17.1

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Documentation

- Purpose
- Tiers of documentation
- Procedures and Instructions
- Records and Reports
- Format of Documents
- Creating a Documentation System

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Documentation

General Principles – I

- Documentation is an essential part of QA and relates to all aspects of GMP
- Purpose of documentation
  - to ensure that there are specifications for all materials and methods of manufacture and control
  - ensure all personnel know what to do and when to do it
  - ensure that authorized persons have all information necessary for release
  - provide audit trail

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Documentation

General Principles – I

- Documents should be
  - designed
  - prepared
  - reviewed
  - distributed with care
- Design of documentation

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Documentation

General Principles – II

- look at the "Style" of the document
  - Instructions in the imperative
  - Short sentences
  - Not long sentences

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Documentation

General Principles – III

- Approval of documentation
  - Approved, signed and dated by appropriate authorized persons
  - No document should be changed without authorization

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Documentation

General Principles – IV

- Distribution of documentation:
  - Electronically, or
  - photographically recorded data, or
  - Hard copies

➢ Or combinations!

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Documentation

General Principles – V

- Review
  - system for regular revision

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Documentation - Purpose

- To describe all manufacturing activities
- To ensure activities are carried out exactly the way they have been planned and approved
- To achieve conformity and quality improvement
- To relate the history of these activities
- To prevent risks of interpretation
- To prevent loss of information, confusion or errors inherent of verbal communication

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Documentation - Purpose

Benefits!

- Specifications for all materials and methods of manufacture and control are set
- Employees know what to do
- Responsibilities and authorities identified
- Authorized persons have all information necessary for release
- Provide audit trail
- Forms the basis for improvement

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Documentation – Creating a System

A documentation system should allow CAREFUL…

- Design
- Preparation
- Management
- Review
- Distribution

…of documents

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Documentation – Creating a System

A well-designed documentation system ensures:

- Complete history of each batch – traceability
- From starting materials → finished products
- Records present for – maintenance, storage, QC, immediate distribution, issues related to GMP

Documents are legal evidence!

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Documentation – Creating a System

Document Content:

- Name of doc
- Name of company, department / function
- Doc #
- Page X of Y
- Names & Signatures of Author & Reviewer/Approver
- Approval date; Revision date
- Body of text
- Document received, if applicable

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Documentation – Creating a System

Hand written entry:

- Signed & dated
- Permanent ink
- Correction: Single line across original entry (so it is still legible) → write new entry close to original entry → initial & date correction (with reason, if appropriate)

Computerized?

- Password
- Assigned person

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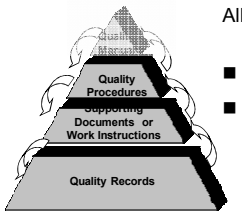
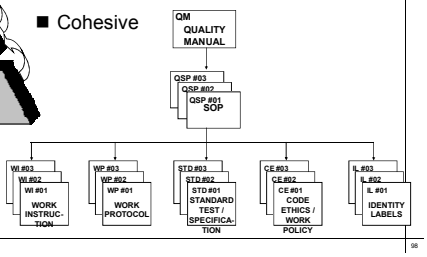
Documentation – Tiers



All levels are integrated & cross referenced so the all documents are:

- Comprehensive
- Cohesive



98

Documentation – Tiers

SOP (Standard Operation Procedures)…

…describe detailed explanation on how activities should be performed, controlled and recorded

SOP Contents:

- The process & its purpose
- Location(s) to perform process
- Personnel responsible for every step
- How to complete the process – instructions or reference to instruction documents e.g. WI
- How to record information / data
- Frequency of the process

99

Documentation – Tiers

Supporting Documents or Work Instructions

WI (Work Instructions)…

… describe step-by-step instructions specifying how the activities are performed or products are accepted.

WI Contents:

- Explanation of instructions to finish a task, detailed handling and method for equipment and machine
- Technical provisions for operation, inspection and testing
- May contain – worksheet, sample, checklist, illustration, photo etc

100

Documentation – Tiers

SOP

- **Focus: Process**
- Steps of procedure
- General description on process
- Gives systematic action to ensure product quality
- Guideline which may involved several departments / functions
- Reference to supporting documents during implementation
- At organisational level

Supporting Documents or Work Instructions

- **Focus: Task**
- Detailed instructions
- Guidance on operation
- Explain special task, method, or technique
- Instruction for certain department / function
- Stand alone instruction during a process
- At operational level

101

Documentation – Tiers

Quality Records

Records…

… are evidence for the processes & tasks carried out. These can be charts, data, inspection & audit reports, testing results etc…

Records should be:

Supporting Documents or Work Instructions

- Legible & Complete
- Accurate & factual
- Dated – Real-time records
- Reviewed & approved
- Retained for defined period
- Protected from deterioration in storage

102

Documentation

Types of Documentation

- Labels, specifications and master formulae
- Batch processing and batch packaging records
- Standard operating procedures
- Stock control and distribution records
- Water quality manual
- Other types; f.e. waste containers

103

Documentation – Format

Detailed, but written in simple language that can be understood by the user.

Ways to express what needs to be done:

- Narrative
- Flowchart
- Combination

104

Documentation – Format

Narrative – most common

Include:

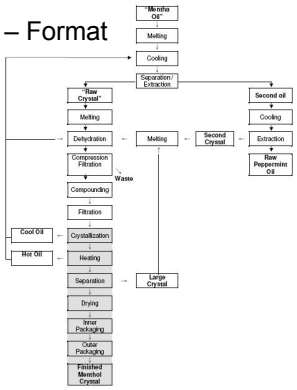
- Objective – what is this document for?
- Coverage area – scope
- Document reference – SOP #, version
- Responsible person
- Detail procedure
- Record, if applicable

105

Documentation – Format

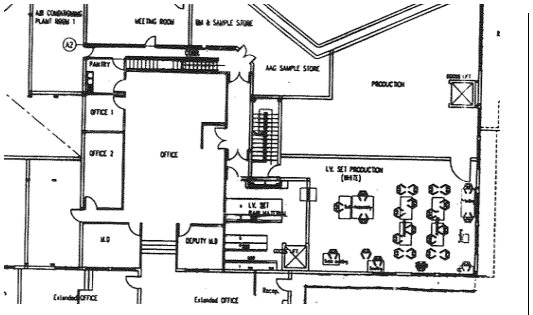
Flowchart

- Schematic description of the process flow
- Clear and easy to read and follow
- Often used in combination with narrative to enhance understanding → lower risk of error



The processes in shaded texts, i.e. after Filtration, occur in the cleanroom environment (class 300,000).

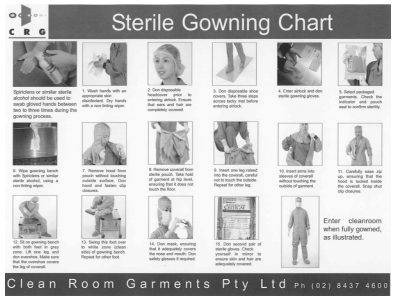
Documentation – Format



107

Documentation – Format

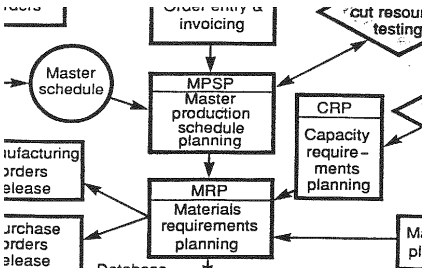
- Photo-graphs are useful additions to documents



108

Documentation – Format

- Flow charts provide substantial information at a glance

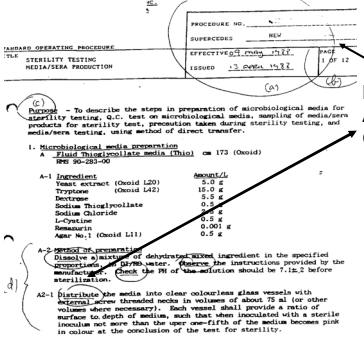


Documentation – Format

Labels

- What must be labelled?
- What must be on the label?
- Who has responsibility for labelling?

Documentation – Format



No unsigned And undated Changes!!!

No pencils!!

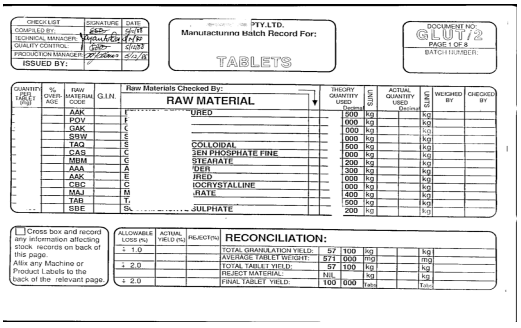
No correction Fluids!!

Documentation – Format

Specifications and Test Procedures

- Starting and packaging materials
- Intermediates and bulk products
- Finished products

Documentation – Format



CHECK LIST	SIGNATURE	DATE
COMPILED BY:		
TECHNICAL MANAGER:		
QUALITY CONTROL:		
PRODUCTION MANAGER:		
ISSUED BY:		

PTY.LTD.
Manufacturing Batch Record For:
TABLETS

DOCUMENT NO:
GLU12
PAGE 1 OF 8
BATCH NUMBER:

QUANTITY PER UNIT	% OVER-AGE	RAW MATERIAL CODE	G.L.N.	Raw Materials Checked By: RAW MATERIAL	THEORY QUANTITY USED Decimal	UNIT	ACTUAL QUANTITY USED Decimal	UNIT	WEIGHED BY	CHECKED BY
		AAK		URED	500	kg		kg		
		POY			000	kg		kg		
		OAK			000	kg		kg		
		SSW			000	kg		kg		
		TAG		COLLOIDAL	500	kg		kg		
		CAS		EN PHOSPHATE FINE	000	kg		kg		
		MHM		STEARATE	200	kg		kg		
		AAA		DER	300	kg		kg		
		AAK		RED	000	kg		kg		
		CSC		OCRYSTALLINE	000	kg		kg		
		MAJ		RATE	400	kg		kg		
		TAB			500	kg		kg		
		SBE		SULPHATE	200	kg		kg		

☐ Cross box and record any information affecting stock records on back of this page.
Affix any Machine or Product Labels to the back of the relevant page.

ALLOWABLE LOSS (%)	ACTUAL YIELD (%)	REJECT(%)	RECONCILIATION:						
± 1.0			TOTAL GRANULATION YIELD:	57	100	kg		kg	
			AVERAGE TABLET WEIGHT:	571	000	mg		mg	
± 2.0			TOTAL TABLET YIELD:	57	100	kg		kg	
			REJECT MATERIAL:	NIL		kg		kg	
± 2.0			FINAL TABLET YIELD:	100	000	Tablets		Tablets	

Documentation – Format

Master Formulae I

- Manufacturing instructions
  - Name of product with product reference code
  - batch size
  - Full list of materials including quantities; unique reference code
  - Expected final yield with acceptable limits (+intermediate yields)
  - Processing location and principle equipment

Documentation – Format

Master Formulae II

- Manufacturing instructions - continued
  - Equipment preparation methodology
  - Stepwise processing instructions
  - Details of in-process controls with instructions for sampling and acceptance limits
  - Storage requirements and special precautions.

115

Documentation – Format

Master Formulae III

- Packing instructions
  - Name of the product
  - Pack size (number, weight or volume of product in finished pack)
  - List of all packaging materials (quantities, size and code number)

116

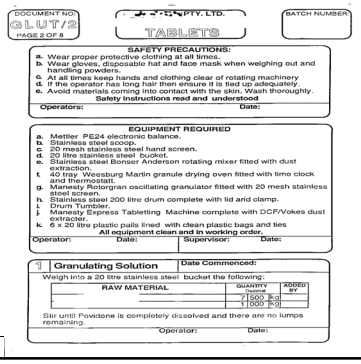
Documentation – Format

Master Formulae - IV

- Packing instructions - continued
  - Examples of printed packaging materials, with location of batching information
  - Special precautions, including area clearance checks
  - Description of the packaging operation
  - In-process control checks, with sampling instructions and acceptance criteria

117

Documentation – Format



DOCUMENT NO: GLUT/2 PAGE 2 OF 8

PTY. LTD.

TABLETS

BATCH NUMBER

SAFETY PRECAUTIONS:

a. Wear proper protective clothing at all times.
b. Wear gloves, disposable hat and face mask when weighing out and handling powders.
c. At all times keep hands and clothing clear of rotating machinery
d. If the operator has long hair then ensure it is tied up adequately.
e. Avoid materials coming into contact with the skin. Wash thoroughly.

Safety instructions read and understood

Operators: Date:

EQUIPMENT REQUIRED

a. Mettler PE24 electronic balance.
b. Stainless steel scoop.
c. 20 mesh stainless steel hand screen.
d. 20 litre stainless steel bucket.
e. Stainless steel Bonser Anderson rotating mixer fitted with dust extraction.
f. 40 tray Weesburg Martin granule drying oven fitted with time clock and thermostatt.
g. Manesty Rotorgran oscillating granulator fitted with 20 mesh stainless steel screen.
h. Stainless steel 200 litre drum complete with lid arid clamp.
i. Drum Tumbler.
j. Manesty Express Tabletting Machine complete with DCF/Vokes dust extracter.
k. 6 x 20 litre plastic pails lined with clean plastic bags and ties

All equipment clean and in working order.

Operator: Date: Supervisor: Date:

9 **Granulating Solution** Date Commenced:

Weigh into a 20 litre stainless steel bucket the following:

RAW MATERIAL	QUANTITY	ADDED BY
	7 500 gm	
	1 000 gm	

Stir until Povidone is completely dissolved and there are no lumps remaining.

Operator: Date:

Documentation – Format

Batch Processing Records - I

- Name of the product, batch number
- Dates and times for major steps in process
- Name of person responsible for each stage of production
- Name of operators carrying out each step (check signatures)
- Theoretical quantities for materials in the batch
- Reference number and quantity of materials used in the batch

Documentation – Format

Batch Processing Records - II

- Main processing steps and key equipment
- In-process controls carried out, and results obtained
- Yield at each stage with comments on deviations
- Expected final yield with acceptable limits
- Comments on any deviations from process.
- Area clearance check, instructions to operators
- Record of activities

Documentation – Format

Batch Packaging Records - III

- Name of the product, batch number and quantity to be packed
- Batch number, theoretical quantity and actual quantity of finished product
- Reconciliation calculations, dates and times of operation
- Name of person responsible for packaging, initials of operators carrying out each step
- Checks made and results obtained

121

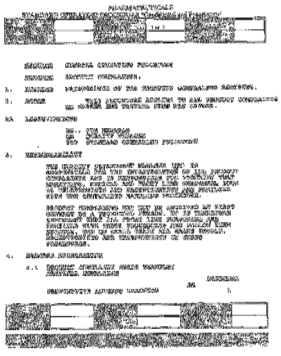
Documentation – Format

Batch Packaging Records - IV

- Details of packaging operation, including equipment and line used
- Returns to store
- Specimen of printed packaging materials, with batch coding
- Comments on deviations from the process and actions taken
- Reconciliation of packaging materials, including returns and destruction
- Area clearance check
- Product variables
- Record of activities and check signatures

122

Documentation – Format



123

Documentation – Format

Standard Operating Procedures - I

- Who is responsible for SOPs?
- Where should SOPs be stored?

124

Documentation – Format

Standard Operating Procedures - II

- Which activities require SOPs?
  - Receipt of all material deliveries
  - Internal labelling, quarantine and storage of materials
  - Operation, maintenance and cleaning of all instruments and equipment
  - Sampling of materials
  - Batch numbering systems
  - Material testing at all stages of production

125

Documentation – Format

Standard Operating Procedures - III

- Which activities require SOPs? - continued
  - Batch release or rejection.
  - Maintenance of distribution records
  - Equipment assembly and validation
  - Calibration and operation of analytical apparatus
  - Maintenance, cleaning and sanitation
  - Personnel recruitment, training, clothing and hygiene
  - Environmental monitoring

126

Documentation – Format

Stock Control and Distribution Records

- What should be recorded?
- Where should records be stored?
- Why are the records important?

127

Materials Management

"This has been in the sun for a couple of days, but it passed all tests just a week ago. Shall I use it anyway…?"

WHEN YOU NEED TO BE SURE

Materials

Materials can be:

- Raw Materials
- Packaging Materials

They should all have defined acceptance criteria!

In other words – specifications.

129

Materials

Key steps:

- Purchasing
- Receipt & Recording
- Sampling & Testing
- Accept & Release / Reject
- Storage
- Oldest Used First
- Reconciliation & Inventory

130

Materials

Purchasing

Have you…?

- Selected your supplier through evaluation?
- Specified the type of evaluation e.g. questionnaire, audits?
- Set acceptance criteria for the items?
- Established actions in case of defect or modifications?
- Set transport conditions?

131

Materials

Receipt & Recording

- Check if intact visually + transport data
- Check if received item is what you ordered

"*The purchase order, the delivery note and the delivered materials should match.*"

ISO 22716:2007 – 6.3.1

Yet more required documents:

- PO
- DN
- Record of checking these 2 should match

132

Materials

Receipt & Recording

- Label to show identity
  - Name/code of material
  - Batch number
- Label / Physical System to show status
  - Quarantined
  - Accepted
  - Rejected

133

Materials

Receipt & Recording

- One set of label to fulfill “ID” & “Status” clarity…

Name of Material	
Internal Code	
Batch No /	
Receiving No.	
Status	Quarantine / Release Rejected / Hold
Expiry Date	Retest Date
Receiving Date	
Signature	

134

Materials

Receipt & Recording

Name of Material	
Internal Code	
Batch No /	
Receiving No.	
Status	Quarantine
Expiry Date	Retest Date
Receiving Date	
Signature	

Name of Material	
Internal Code	
Batch No /	
Receiving No.	
Status	Rejected
Expiry Date	Retest Date
Receiving Date	
Signature	

Name of Material	
Internal Code	
Batch No /	
Receiving No.	
Status	Release
Expiry Date	Retest Date
Receiving Date	
Signature	

Name of Material	
Internal Code	
Batch No /	
Receiving No.	
Status	Hold
Expiry Date	Retest Date
Receiving Date	
Signature	

135

Materials

Sampling & Testing

A sampling procedure to specify:

- Sampled containers identification
  - sample _ of _
  - taken by ___ department
  - taken by _____
  - quantity taken _____
- Testing accorded to specification

136

Materials

Accept & Release

- Checked and verified for their conformity to specifications
- Released by authorized personnel from Quality
- "… *can be accepted on the basis of supplier certificate of analysis only if there are established technical requirements, experience and knowledge of the supplier, supplier audit and agreed supplier's test methods."*

ISO 22716:2007 – 6.5.3

137

Materials

Storage

- According to appropriate conditions
- Conditions controlled, monitored & recorded
- Containers should be closed & stored off the floor
- Orderly – avoid mix up & cross contamination
- FIFO & FEFO
- Periodic inventory

138

Materials

Reject

OOS / Expired stock – Reject

- Clearly marked
- Segregated and Access controlled
- Returned to supplier / Destroyed / Reprocessed according to SOP
- Any of these actions --- approved by authorized personnel from Quality Unit
- Record the action

139

Materials

One thing worth mentioning:

- Re-evaluation System
  - After a defined period of storage
  - Exposed in sun
  - Exposed in heat
  - Exposed to air
  - Etc
- If in doubt of its quality…

140

Materials

Water Quality used in Production

- The water treatment system should supply a defined quality of water
- Water quality should be verified by either testing or monitoring process parameters
- Sanitization of water treatment system
- Water treatment equipment – avoid stagnation and risks of contamination
- Materials in water treatment equipment – does not affect water quality

141

Materials

Objectives

- To review specific requirements for each type of material:
  - Starting materials
  - Packaging materials
  - Intermediate and bulk products
  - Finished products
  - Rejected and recovered materials
  - Recalled products
  - Returned goods
  - Reagents and culture media
  - Reference standards
  - Waste materials
  - Miscellaneous materials.
- To examine the problems associated with materials, and how to overcome them.

142

Materials

General requirements for materials

- All incoming materials and finished products:
  - quarantined after receipt,
    - until released for use
    - distribution
  - stored
    - under appropriate conditions
    - orderly fashion (batch segregation)
    - materials management
    - stock rotation (FIFO or EEFO))

143

Implementing ISO 22716

- **Selection of suppliers of raw materials & Packaging materials (6.2.a and 6.5).**
  - Under GMP the selection of suppliers of raw materials and all other materials and supplies used for the manufacturing of cosmetic products needs to be done following written and approved procedures as defined by the organization, following clear quality guidance based upon a proper risk assessment. Based upon this procedure a once approved supplier cannot be changed on financial terms but needs to go through a similar qualification program as set earlier for the original supplier (following a change control program). The organization needs to have a written, controlled, and quality-approved list of approved suppliers.

144

Materials

Starting Materials – I

- Purchasing
- Suppliers
- Consignment:
  - integrity
  - seal
  - order
  - delivery note
  - supplier's labels
- Cleaned and labelled

145

Materials

Starting Materials – II

- Damaged containers
- Different batches in one consignment
- Starting material label:
  - name and internal code
  - batch number(s), (supplier and manufacturer on receipt)
  - status
  - expiry date or re-test date
- Sampled containers identified

146

Materials

Examples of Labelling of Starting Materials

Name of Material and/or internal code			
Control/ Batch No.			
Status	**Quarantined/Released/Rejected (Colors may be used)**		
Expiry date or retest date			
Date		Signature	

147

Materials

Starting Materials – III

- Use only released material
- Dispensing:
  - designated persons
  - written procedure
  - accurately weighed
  - clean, labelled containers
- Independent checks
  - material and weight
- Dispensed material:
  - kept together and labelled

148

Materials

Packaging materials I

- Primary and printed materials:
  - as for starting materials
    - purchasing, handling and control
- No unauthorized access of storage area
- Storage and transport
  - avoid mix-ups
  - issue and return: SOP

149

Materials

Packaging materials II

- Specific reference number for batch or consignment
- Packaging department checks:
  - quantity, identity and conformity
- Outdated or obsolete material

150

Materials

Intermediate and bulk products

- Appropriate conditions
- Purchased:
  - as starting materials

151

Materials

Reagents and culture media

- Recorded upon receipt or preparation
- Reagents:
  - preparation in accordance with SOP
  - label:
    - *concentration, standardisation factor, shelf-life, date that re-standardisation is due, storage conditions*
    - *signed and dated*
- Culture media:
  - positive and negative controls

152

Materials

Waste materials and miscellaneous materials

- Waste materials
  - proper and safe storage
  - toxic and flammable materials
    - separate, enclosed, as per legislation
  - not allowed to accumulate
    - collected for safe disposal
    - regular intervals
- Miscellaneous
  - rodenticides, insecticides, sanitizing material
  - contamination risks

153

GMP (Good Manufacturing Practice) for Cosmetic Products

End of section 4

WHEN YOU NEED TO BE SURE SGS

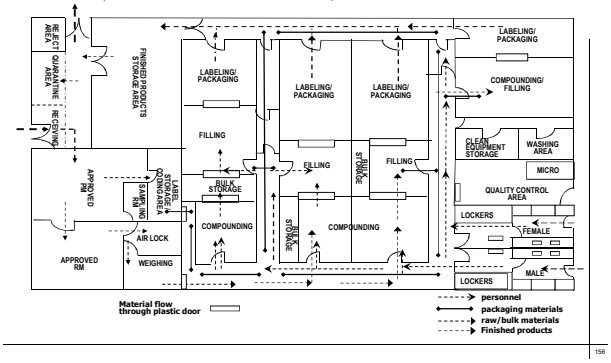
Premises

Design

- Flow of materials, products and personnel through the building
- Adequate space for all operations
- Smooth/crack-free/easy to clean interior surfaces
- Separate defined areas for:
  - Storage
  - Production
  - Quality control
  - Washing and toilets

155

Premises – example



156

Premises

Construction

4 topics:

- Floors
- Walls
- Ceilings
- Windows

157

Premises

Construction

- Floors

Production

- Solid concrete with epoxy or polyurethane resin finish (it has non-porous topping with non-skid surface & decreases bacterial growth!

Warehouse

- Solid concrete

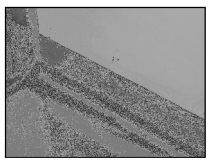
Cleaning & Sanitizing Procedures!

158

Premises

Construction

- Walls



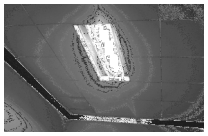
High density, smooth plaster, waterproofed by painting acrylic / high polymer enamel

159

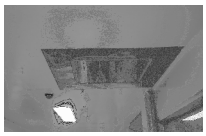
Premises

Construction

- Ceilings



With joint…



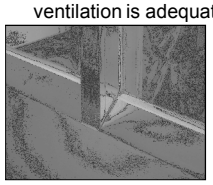
Without joint!

160

Premises

Construction

- Windows – should be non-opening (where ventilation is adequate)



Key:

The way it fits into the frames

The way the frames fit into the wall

It should allow:

- Easy cleaning and sanitation!

161

Premises

Construction

All surfaces should have resistance to corrosive cleaning and sanitizing agents.

162

Premises

Cleaning

Another required document:

A Cleaning Programme

- Cleaning / sanitizing agents &/or materials
- Cleaning frequency
- Cleaning method / duration
- Effectiveness of these agents assessed & monitored
- FOR EACH AREA

163

Premises

Ventilation

"…should be sufficient for the intended production operations."

- Air to be filtered in the processing and filling areas:
  - One pass filtration air or circulation for wet, non-powdered and dry preparations
  - A dust collection system for dry or powdered product

164

Premises

Pipework, drains and ducts

No contamination from drip or condensation!

- Avoid exposed overhead beams, pipes and ducts
- Sufficient separation of exposed pipes and walls – use brackets, so to allow cleaning
- Drains – must not allow back flow

165

Premises

Pest Control

Another document ISO requires:

A Pest Control Program

- To restrict access to insects, birds, rodents, pests and other vermins
- Also should control the exterior of the premises to prevent attracting or harbouring pests

166

Equipment

It could be…

- Mixer
- Dryer
- Centrifuge
- Temperature recorder
- Balance
- Testing equipment in QC lab
- Particle counter
- MORE …

167

Equipment

Think the direction as Premises:

- Suitability to its intended purpose
- Designed to prevent contamination – between batches; between products; of products by personnel or by environment
- Capabilities to allow effective cleaning
- Construction Materials – stable and compatible with cleaning agents
- Maintenance

168

Equipment

In addition to Premises:

- Surface Materials – stable and compatible with products
  - Not reactive
  - Not additive
  - No adsorptive Capable of producing valid results
- Operated by trained personnel
- Installation
- Calibration

169

Equipment

In addition to Premises:

- Surface Materials – stable and compatible with products
  - Not reactive
  - No adsorptive Capable of producing valid results

Some examples:

- 316L stainless steel – pipelines
- Plastic maybe cheaper – but unstable with hot sanitation; surface may not be smooth

170

Equipment

Installation

- Avoid congestion – allow movement of materials, mobile equipment and personnel
- Properly identified
- Easy access under, inside and around the equipment

Reasons:

- Minimize risks of contamination and to quality
- Allow effective cleaning
- Allow effective maintenance

171

Equipment

Calibration – regular!

- Calibration Frequency depends on
  - Type of equipment
  - Frequency of use
  - Important in manufacturing process

Some examples:

Air pressure regulator

Pressure gauge & release valve

172

Equipment

Calibration – OOS

- Follow OOS procedure of company for that equipment
- Identify it as OOS equipment – label etc
- Removed from service!

Reason:

- The data an OOS equipment produces is not reliable!

173

Equipment

Calibration

- Calibration Labels – typical to a manufacturing plant

Some examples:

Calibration date: _____
By: _____
Due: _____

Calibration ID No.
_____

Calibration Void If Broken

Calibration Void DO NOT USE

Not a Calibration Instrument

174

Equipment

Maintenance

- Have an equipment list
- Have a written schedule – servicing, cleaning, calibration
- Document the maintenance activities

175

Facility Design and Engineering

UPPER Blend vessels / Utility (Tech)

LOWER Buffer/Media Prep / Clean Corridor with autoclave


176

The manufacturing environment is critical for product quality

- Light
- Temperature
- Humidity
- Air movement
- Microbial contamination
- Particulate contamination
- Uncontrolled environment can lead to product degradation
  - *product contamination*
  - *loss of product and profit*

177

What are contaminants ?

1. **Products or substances other than product manufactured**
2. **Foreign products**
3. **Particulate matter**
4. **Micro-organisms**
5. **Endotoxins (degraded micro-organisms)**

178

Cross-Contamination (1)

Definition of Contamination:
The undesired introduction of impurities of a chemical or microbiological nature or foreign matter into or onto a raw material, intermediate or excipient during production, sampling, packaging or repackaging, storage or transport.

Definition of Cross-Contamination:
Contamination of a material or product or batch with material or product or batch during production.

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Cross-Contamination (2)

From where does Cross-Contamination originate?

1. Poorly designed air handling systems and dust extraction systems
2. Poorly operated and maintained air handling systems and dust extraction systems
3. Inadequate procedures for personnel and equipment
4. Insufficiently cleaned equipment

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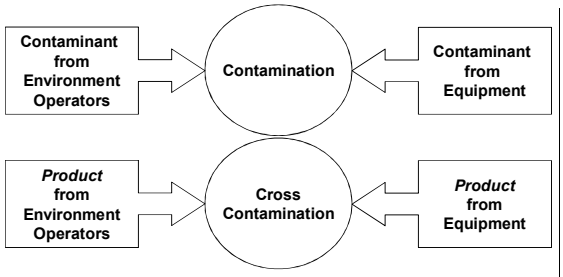
Cross-Contamination (3)



181

Cross-Contamination (4)

Cross-contamination can be minimized by:

1. Personnel procedures
2. Adequate premises
3. Use of closed production systems
4. Adequate, validated cleaning procedures
5. Appropriate levels of protection of product
6. Correct air pressure cascade

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Parameters influencing Levels of Protection (2)

1. Number of particles in the air
2. Number of micro-organisms in the air or on surfaces
3. Number of air changes for each room
4. Air velocity
5. Air flow pattern
6. Filters (type, position)
7. Air pressure differentials between rooms
8. Temperature, humidity

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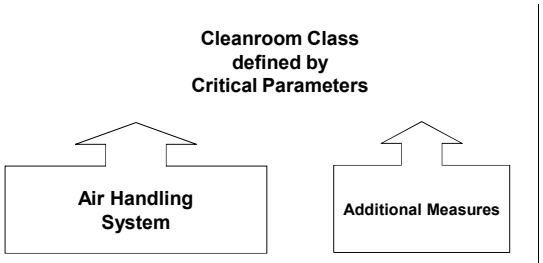
Parameters influencing Levels of Protection (3)



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GMP (Good Manufacturing Practice) for Cosmetic Products

End of Section 3

WHEN YOU NEED TO BE SURE

GMP (Good Manufacturing Practice) for Cosmetic Products

Section 5: Production and Quality Control

WHEN YOU NEED TO BE SURE

GMP Section 5 - Outline

With reference to ISO 22716 as basis:

- Production
- Quality Control

187

Production

Objectives

- To manufacture products of good quality and safety
- To standardize all production activities
- To ensure consistency by using only approved starting materials
- To identify & record production activities – traceability
- To avoid contamination & cross contamination
- To avoid error

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Production

Examples of activities:

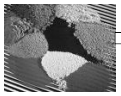
- Weighing
- Cleaning & sanitization
- Preparation of bulk products
- Filling
- Packing
- Reconciliation of product output
- Recording of each activities
- Quarantine and delivery to warehouse
- Reprocessing, if necessary

189

Production

Map Your Production Steps!

Production operations must follow clearly defined procedures + approved specifications.


Raw Material


Weighing


Processing

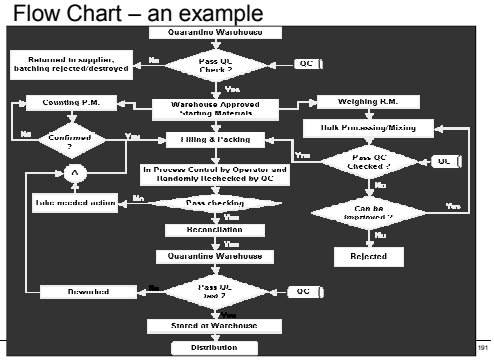

Filling & Packing

Bulk Storage


Delivery to Warehouse

Production

Flow Chart – an example



Production

Before you start…

- Relevant documentation available

- Starting materials must be tested and approved / released

- Equipment is available for use, in working order, cleaned / sanitized

- CLEARANCE of the area has been performed to avoid mixing with materials from pervious operations

Production

Have a start-up checklist…

- ☑ Sections 2,3 & 4 of the BPR

- ☑ Raw material 30kg x RM258, 20kg x RM107 released
- ☑ Purified water system in spec

- ☑ Mixer B201, dryer B312, balance B283, pipette QC021 – clean, valid, in order

- ☑ Room 101 – 106 in Area B checked – no material from previous operations left or material not relevant to this operation
- ☑ Room 101 – 106 in Area B cleaned within 2 days before this operation

193

Production

Assigning Batch Number

- "*A batch number should be assigned to each batch of manufactured bulk product. This number does not need to be identical with the batch number that appears on the label of the finished product, but, if not, it should be easy to relate to that number.*"
- ISO 22716:2007 – 7.2.3

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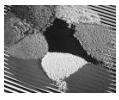
Production



Raw Materials

- Must be approved

Weighing

- In defined areas
- Using calibrated equipment
- Recorded
- Counter checked by second person

195

Production

In-process Control

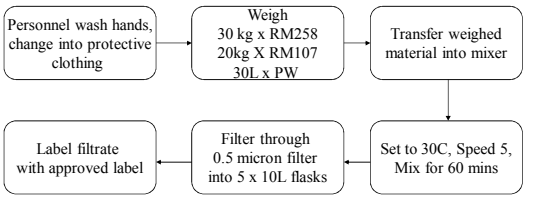
- Identify the critical steps of the whole operation
- Define the control mechanisms for these critical steps – define acceptance criteria
- Write all these in-process control points in a defined programme
- Implement the in-process control programme
- Any OOS result – reported and investigated!

196

Production

In-process Control Programme

- What steps would you mark critical and why?



Where In-process Control?

197

Production

In-process Control

- Done within the production area by production and/or Quality personnel
- Recorded and done as per SOP
- Sampling done to verify:
  - Physical aspects (e.g. weight, volume, amount etc)
  - Temperature
  - Microbial load
- Sampling can be:
  - Random
  - Sequential, or
  - Statistical

198

Production

Bulk Product Storage

- Suitable containers
- Labeled with sufficient info for identification
- In defined areas
- Under appropriate conditions
- With defined maximum storage period
- If maximum period reached → re-evaluation before use

199

Production

Filling and Packaging

CLEARANCE again!

- ☑ Sections 5 of the BPR
- ☑ Packaging material – 30 x 5ml PP bottle & lid; 30 x label A, 30 x label B
- ☑ Filling, packing, labeling machines – clean, valid, calibrated, in order
- ☑ Room 107 in Area B checked – no material from previous operations left or material not relevant to this operation; cleaned within 2 days prior

200

Production

Filling & Packing also needs:

In-process Control

- Identify the critical steps of the whole operation
- Define the control mechanisms for these critical steps – define acceptance criteria
- Write all these in-process control points in a defined programme
- Implement the in-process control programme
- Any OOS result – reported and investigated!

201

Production

Filling & Packing

Tips 1 of 2

- Avoid filling & packing of different products in close proximity unless physical segregation sufficient
- Packaging line should bear product name & batch number being produced
- Verification of correct performance of printing done separately, checked and recorded
- Special care should be taken when cut labels are used

202

Production

Filling & Packing

Tips 2 of 2

- Samples taken away from the packaging line once opened should not return
- Any unusual discrepancy during reconciliation should be investigated before product release
- Any unused batch-coded materials should be destroyed and recorded
- Excess labels and packaging materials should be returned to store; properly tagged/labeled and recorded

203

Implementing ISO 22716

- **Line-clearance of packaging (7.3.2).**
  - All materials of a previous batch have to be removed from the packaging line. For example (but not restricted to) labels, leaflets, inserts, carton boxes, bottles, etc. etc. The line clearance has to be clearly referenced in the batch record (and room log book) and preferably has to follow a checklist (as defined in the SOP on line clearance) on the items (equipment, room) to check for left-overs of the previous product or batch.

204

Packaging line segregation

- Separate room
- One batch of one product per line
- Uni-directional flow

205

Production

Reconciliation

- Yields and Reconciliation of quantities – checked
  - Quantity of starting materials
  - Output of finished products
  - Machine efficiency
  - Etc
- Set defined acceptable limits – spec
- OOS → investigate
- All reconciliation activities – against SOP

206

Production

Types of products

- Dry
- Semi solid
- Wet

207

Production

Dry Products

Cautions

- Cross contamination
- Contamination from air, equipment, facilities

Solution

- Use dust collector in weighing are, mixing/blending room, and in filling/packaging
- Anti-room with air lock in between
- Environmental control, temperature & humidity
- Dedicated personal protective safety equipment for operators

208

Production

Semi Solid Products

Cautions

- Over heating during mixing & heating
- Homogeneity of color
- Cross- and contamination

Solution

- Check color conformity
- Check melting point & breaking point
- Microbiological test

209

Production

Wet Products

Cautions

- Cross- and contamination
- Leakage of system

Solution

- Closed system – avoid contamination
- Clean pipes for transfer
- Avoid dead end / dead legs on piping

210

Production

FINISHED PRODUCTS

211

Production

Finished Products

Principle:

"… *should meet the defined acceptance criteria.*

Storage, shipment and returns should be managed in a manner so as to maintain the quality of finished products."

ISO 22716:2007 – 8.1

212

Production

Finished Products

Release

- Tested against established test methods
- Test results meet acceptance criteria
- Release carried out by authorized personnel responsible for quality

213

Production

Finished Products

Identification

- Name or identifying code
- Batch number
- Storage conditions when such info is critical to assure quality of product
- quantity

Production

Finished Products

Storage & Shipment

- Stock number control – FEFO
- Periodic inventory – discrepancy → investigate
- Precautions to be taken to maintain quality of the finished product.

Production

Finished Products – Example Stock Card

COMPANY NAME : FINISHED PRODUCT STOCK CARD

PRODUCT NAME : CODE NO :

UNIT :

IN				OUT				
Date	Report No	Batch No	Qty	Date	Batch No	Distributor	Qty	Remaining

Production

Finished Products

Retained Samples in separate archive

For reference and retesting for stability evaluation and in case of product complaint.

217

Production Document

For each cosmetic product:

- Master Formula
- Batch Manufacturing / Production Record (BMR / BPR)
- Record of Quality Control

218

Production Document

BPR should include:

- Name of product
- Batch formula
- Brief manufacturing process
- Batch or code number
- Date of start and finish of processing and packaging
- Identity of individual major equipment and lines or locations used
- Records of cleaning & sanitation of equipment
- In-process control & lab results
- Line clearance record
- Any sampling
- Any investigation
- Results of examinations on packed and labeled products

219

Quality Control Laboratory

"This bottle of liquid does not bear any labels, what is this…? I hope it's not sulphuric acid!"

WHEN YOU NEED TO BE SURE SGS

QC Laboratory

Principle

"*The quality control laboratory is responsible for ensuring that the necessary and relevant controls, within its activity, are carried out for sampling and testing so that materials are released for use and products are released for shipment, only if their quality fulfuils the required acceptance criteria."*

ISO 22716:2007 – 9.1.2

221

QC Laboratory

"Quality control involves sampling, inspecting and testing of starting materials, in-process, intermediates, bulk, and finished products.

It also includes where applicable, environmental monitoring programs ."

ASEAN 7.1.1

222

QC Laboratory

Attached to manufacturing unit, but separate from production!

What does a QC Lab involve?

223

QC Laboratory

Sampling	Sample Retention Program	Reagent Handling
Inspection & Testing of Samples	Stability Study	Specifications
EM Program	Calibration	Release, Reject

224

QC Laboratory

QA vs QC

Assurance	Control
Giving confidence All planned and systematic activities implemented within the quality system that can be demonstrated to provide confidence a product or service will fulfill requirements for Quality	Evaluation The operational techniques and activities used to fulfill requirements for Quality

225

Implementing ISO 22716

- **What is an appropriate test method? (9.2.2).**
  - ISO22716 does not require full validation of quality control test methods (like in Pharma). At least the organization under ISO22716 needs to do an assessment on the suitability of the test method they're using to verify the quality status of a finished product. This can be done by comparing several tests intending to measure the same parameter with each other and write down a relevant and suitable conclusion or by using literature references or otherwise well accepted test methods to deliver proof that a given method can be implemented in a similar case on their site.

226

Accepted test methods

- For example:
  - ISO 24444:2010; Cosmetics -- Sun protection test methods -- In vivo determination of the sun protection factor (SPF)
  - ISO 10130:2009; Cosmetics -- Analytical methods -- Nitrosamines: Detection and determination of N-nitrosodiethanolamine (NDELA) in cosmetics by HPLC, post-column photolysis and derivatization

227

QC Laboratory

Basic Requirements 1 of 2

Test methods

- Test methods defined for all necessary tests with acceptance criteria
- Controls performed on the basis of defined, appropriate and available test methods

Acceptance Criteria

- Established to specify requirements to be met for raw materials, packaging materials, in-process, intermediate, bulk products and finished products

228

QC Laboratory

Basic Requirements 2 of 2

Results

- Reviewed – then decision made: approval, rejection or pending

OOS Results

- Reviewed by authorized personnel → investigated
- Sufficient justification for any re-testing
- After investigation → authorized personnel makes decision: deviation, rejection or pending

229

QC Laboratory

Other Requirement

Reagents & Retained Samples

- Evaluation, maintenance, storage and monitoring all reference standards, reagents & retained samples

Stability Testing

- Of designated finished product (not all!)

Environmental Monitoring (= establishing of bioburden in manufacturing rooms and laboratories)

- Participation & Conduct

230

QC Laboratory

Reagents, solutions, reference standards, culture media

Identification:

- Name
- Strength or concentration []*
- Expiration date*
- Name / signature of person who prepared it
- Opening date
- Storage conditions*

231

QC Laboratory

Specifications / Acceptance Criteria for:

- Starting materials
- Process water
- Intermediate or bulk product
- Finished product

232

QC Laboratory

Specifications / Acceptance Criteria for:

Starting materials

- Spec should include – designated name, internal code, qualitative and quantitative requirement with acceptance limits

- Other data desired – supplier info, original producer, direction for sampling & testing, storage condition, maximum storage period of storage before re-examination.

233

QC Laboratory

Specifications / Acceptance Criteria for:

Process Water

- Defined standard (ASEAN: potable = minimum)
- Testing at defined intervals & occasions
- Chemical and microbial quality tested / monitored
- Specification – refer to pharmacopeia or supplier design specification

234

QC Laboratory

Specifications / Acceptance Criteria for:

Finished Product

- Designated name, internal code
- Formula number
- Description of finished product and its package details
- Qualitative and quantitative requirement (with limits)
- Direction of sampling and testing, or reference to an approved procedure
- Storage condition or precautions, if any
- Shelf life, if any
- Batch numbering requirement (manufacture / expiry date

235

QC Laboratory

Sampling

Written procedure describing:

- Method & location of sampling
- Equipment to be used – tools and container
- Amounts to be taken
- Any precautions to be observed to avoid contamination or deterioration
- Identification of sample – on container
- Frequency of sampling
- Instruction for cleaning and storage of sampling
- Instruction for re-sealing the opened container

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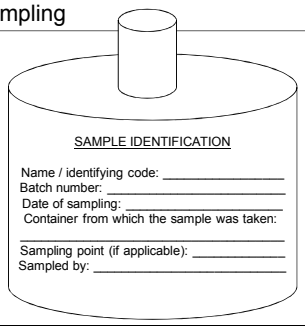
QC Laboratory

Sampling



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QC Laboratory

Sampling

Sampling Plan:

- Raw Material – Sampling plan should be based on defined sampling standard, e.g.:
  - the "*n* plan" is based on the formula n = 1+√*N*, where *N* is the number of sampling units in the consignment;
  - the "*p* plan" is based on the formula *p* = 0.4 √*N*, where *N* is the number of sampling unit; or
  - the "*r* plan" on the formula *r* = 1.5√*N* .
  - reduce sampling plan such as "*p* plan" shall be considered only when there is established confidence on the material's uniformity.

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QC Laboratory

Sampling

Sampling Plan:

- Packaging Materials and Finished Products – Sampling plan should be based on defined sampling standard, e.g.:
  - British Standard BS 6001-1, ISO 2859 pr ANSI/ASQCZ1.4-1993

239

QC Laboratory

Retain Sample

- Taken for finished product
- Sample size should allow analyses to be carried out in accordance with specifications and regulations
- Kept in their primary package for an appropriate time under the recommended storage conditions
- Samples of raw materials may be retained according to company practice or in accordance with local regulations.

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QC Laboratory

Retain Sample

- Taken from finished (labeled and packed) product.
- Sample size should allow analyses to be carried out in accordance with specifications and regulations.
- Kept in their primary package for an appropriate time under the recommended storage conditions.
- Samples of raw materials may be retained according to company practice or in accordance with local regulations.

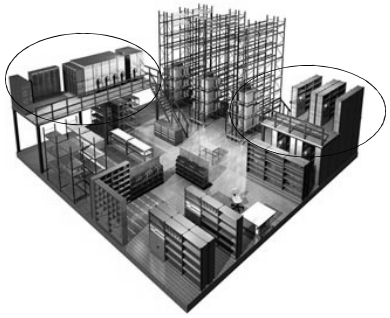
241

Implementing ISO 22716

- **Retain samples (9.8).**
  - The manufacturing organization working under GMP regime according to ISO22716 needs to store samples of each single batch of product they are producing. These are not the regular samples which are analysed during the release of the batch but are kept in storage just in case a problem is arising with the batch of product after bringing into commerce. These so-called retain samples are to be kept in a special retain sample storage facility or room apart from the regular product. The retain samples need to be stored at least until the moment of expiration of the given batch of product. The retain samples need to be stored under similar conditions as compared to the regular product.

242

Separate storage of retain samples



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QC Laboratory

Data – should include…

Lab Report #109

- Results of every test performed – e.g. observations, calculations (even on scratch paper, because this is source data!)
- Source of the specification used
- Signature(s) of the person(s) who performed the procedure
- A final review (e.g. lab manager), the decision taken, and a dated endorsement by an authorized expert (e.g. supervisor / manager)

244

QC Laboratory

Calibration

- Regularly done – calibration schedule & procedure
- Certification to be maintained and reviewed
- If calibration out of acceptance criteria → identified & removed from service
- Out of calibration → investigated to determine any impact to quality of product → if yes, take appropriate actions accordingly
- Document all findings

245

QC Laboratory

Calibration Frequency

- Classification of equipment (Critical? Non-critical?)
- Usage (light or heavy?)
- Handling (light or heavy?)
- Manufacturer's recommendation
- Reference to NIST or accreditation body guideline for a specific measurement system

246

SGS Quality Management

Basic Requirements for Quality Control

Resources

- Adequate facilities
- Trained personnel
- Approved procedures

247

SGS Quality Management

Basic Requirements for Quality Control

Tasks

- Sampling
- Inspecting
- Testing
- Monitoring
- Releasing / rejecting

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SGS Quality Management

Basic Requirements for Quality Control – I

Objects

- Starting materials
- Packaging materials
- Intermediates
- Bulk products
- Finished products
- Environmental conditions

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SGS Quality Management

Basic Requirements for Quality Control – II

1. Sampling approved by QC department
2. Validated test methods
3. Records
4. Review and evaluation of production documentation
5. Failure investigations for all deviations
6. Ingredients comply with the marketing authorization

250

SGS Quality Management

Basic Requirements for Quality Control – III

7. Ingredients are of the required purity
8. Proper containers
9. Correct labelling
10. Release of batches by the authorized person
11. Retained samples of starting materials and products

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SGS Quality Management

Other Duties of the Quality Control Department

1. Establish QC procedures
2. Reference standards
3. Correct labelling
4. Stability testing
5. Complaint investigations
6. Environmental monitoring

252

Quality Management

Assessment of Finished Products

Should embrace all relevant factors. For example:

- Production conditions
- In-process test results
- Manufacturing documentation
- Compliance with finished product specification
- Examination of the finished pack

253

Quality Management

QC Access

- QC Personnel MUST have access to production areas for sampling and investigation
- As appropriate!

254

Quality Management

Quality Control – Summary

QC is part of GMP:

- Sampling
- Specifications
- Testing
- Release procedures
- Recalls and complaints
- Decision-making in all quality matters
- Authorization
- Definition of product quality
- Laboratory operations
- Release decisions
- Investigation and reporting

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GMP (Good Manufacturing Practice) for Cosmetic Products

End of Section 5

WHEN YOU NEED TO BE SURE SGS

GMP (Good Manufacturing Practice) for Cosmetic Products

Section 6: Complaints; Deviations; Returns and recalls; Subcontracting; Internal audits; Documentation

WHEN YOU NEED TO BE SURE SGS

SGS GMP Section 6 - Outline

With reference to ISO 22716 as basis:

- Out-Of-Specification (OOS)
- Deviations, Change Control
- Complaints
- Returns and recalls
- Subcontracting
- Internal audits

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OOS, Deviation, Change Control

"Does it need a change control form? Or… OOS report? Or… a deviation log?"

WHEN YOU NEED TO BE SURE SGS

OOS, Deviation, Change

DEVIATION

Definition

- "internal organization and responsibilities relative to the authorization to deviate from specified requirements due to a planned or unplanned and, in any case, temporary situation concerning one or several activities covered by the Good Manufacturing Practices"

260

OOS, Deviation, Change

Deviations

- Deviations from the specified requirements should be authorized with sufficient data to support the decision
- Corrective action should be made to prevent recurrence of the deviation

261

OOS, Deviation, Change

DEVIATION

Example

- Step 8 of Process B = Mix 1L purified water from water system with 200kg of sodium chloride
- On the day of production, the purified water system was out of order
- Production Head suggested using 1L of bought in & tested WFI instead
- QA Head approved this suggestion – why?

262

Implementing ISO 22716

- **Following up of deviations (10.1.1 & 10.1.2).**
  - Under GMP for ISO22716 each deviation within the supply chain of operations (f.e. but not limited to: purchasing, manufacturing, testing, storage, and transportation) needs to be evaluated and a decision by competent (quality) personnel taken. Appropriate action needs to be done and all relevant steps under deviation control need to be laid down in procedures, protocols, and records. Final decisions done by the relevant quality officer (usually the head of quality) who should have a clear responsibility for this as laid down in the job description. Frequent evaluation of all observed deviations & decisions needs to be done (E.g. by the deviation control team, composed of quality and operations) to keep track of potential deterioration of products.

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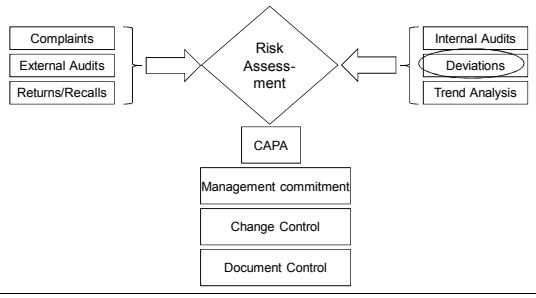
The GMP QA System

How do the systems link together?



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OOS, Deviation, Change

OOS (Out Of Specification)

Definition

- "examination, measurement or test result that does not comply with defined acceptance criteria"

265

OOS, Deviation, Change

OOS (9.5)

OOS results should be:

- Reviewed by authorized personnel
- Investigated --- If retest → sufficient justification for it!
- After investigation → authorized personnel should make a decision → reject or pending → destroy or reprocess

266

OOS, Deviation, Change

OOS (Out Of Specification)

Example

- The acceptance criteria of the number of CFUs for 100ml of a liquid product = 20.
- Test result shows a 100ml sample = 28

267

OOS, Deviation, Change

CHANGE CONTROL

Definition

- "internal organization and responsibilities relative to any planned change of one or several activities covered by the Good Manufacturing Practices in order to ensure that all the manufactured, packaged, controlled and stored products correspond to the defined acceptance criteria"

268

OOS, Deviation, Change

Change Control (15)

- "Changes that could affect the quality of product should be approved and performed by authorized personnel on the basis of sufficient data."

269

OOS, Deviation, Change

CHANGE CONTROL

Examples

- Old blending vessel replaced by new blending vessel
- Changing from supplier A to supplier B for palm oil that is used in manufacturing of shampoo
- Replacing a column in HPLC for laboratory equipment

270

Complaints & Return Policies

"What happened? Which batch did you use? We need to know."

WHEN YOU NEED TO BE SURE SGS

SGS Complaints

A complaint…

"external information claiming a product does not meet defined acceptance criteria"

Definition by ISO 22716:2007

272

SGS Complaints

Objectives

- To identify the key issues in product complaint and recall handling
- To understand the specific requirements for organization, procedures and resources
- To understand and develop actions to resolve current issues applicable to you

273

Complaints

Practices observed at other industries:

Classify them!

Are these complaints on aspects covered by GMP?

- This sun tan lotion doesn't give me a tan.
- The colour of this lipstick is much darker at the bottom.
- I got a rash on my face after using this facial wash.
- This bottle of moisturizer is only half filled! I want my money back!

274

Complaints

A complaint…

- Handled according to an SOP
- Should be centralized
- Concerning product defect – kept with the original details and follow-up information
- Should be followed-up appropriately on the concerned batch
- Should be investigated & follow-up should include

275

Complaints

A complaint…

- Should be investigated & follow-up should include:
  - Steps to prevent recurrence of the defect
  - Checking other batches in order to determine whether they are also affected, where appropriate

Complaints should be reviewed periodically to check for trends or recurrence of a defect.

276

Complaints

"*All complaints that fall within the scope of these guidelines and are communicated to the plant should be reviewed, investigated and followed-up on, as appropriate.*

When a product recall decision is made, appropriate steps should be taken to complete the recall within the scope of these guidelines and to implement corrective action.

In the case of contracted operations, the contract giver and acceptor should agree on the process for managing complaints."

ISO 22716:2007 – 14.1

277

Complaints

Some complaints can lead to a recall …

Some recalls are initiated not due to complaints, but concerns of quality and safety felt by others…

Some recalls are not quality or safety related… examples?

278

Complaints

Complaints Handling Principle

- All complaints and other information concerning potentially defective products must be carefully reviewed according to written procedures
  - Handled positively and carefully reviewed
  - Must be seen as important work
  - Managed by a senior staff member
  - Thorough investigation of the cause is essential
  - A major source of information and learning
  - Enable possible production defects to be remedied before they lead to a recall
  - Necessary actions taken – even a recall decision

279

Complaints

Complaints Procedure – I

- Designated responsible person
  - May be authorized person
  - If not, must advise authorized person of results
  - Sufficient support staff
  - Access to records
- Written procedure describing action to be taken
- Acknowledge and respond to complainant within a reasonable period
- Record written and verbal comments

280

Complaints

Complaints Procedure – II

- Investigate and review
- QA review complaint
- Appropriate follow up actions
- Review of trends

281

Complaints

Records of Complaint Investigation

- Name of product
- Name of active substance (INN) if necessary
- Strength, dosage form
- Batch number
- Name of complainant and nature of complaint
- Records, retention sample investigated, other batches reviewed and staff interviewed
- Result of investigation: “Justified” or “Not justified”
- If “justified”, actions taken to prevent reoccurrence
- Sign-off upon completion

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Complaints

Decision from a Complaint Investigation

- Complaint justified
  - Actions to prevent reoccurrence
  - Ongoing observation of process
  - Recall product may be required
- Complaint not justified
  - Advise customer of findings
  - Appropriate marketing response

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Complaints

Possible Issues – I

- No response to justified complaints
- Response to unjustified complaints
- Failure to recall
- Failure to correct frequent complaints
- No resources to investigate
- No senior management support
- Senior management interference

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Complaints

Possible Issues – II

- No distribution information/batch records
- No access to records
- Inability to contact government during holidays/weekends
- Disagreement on severity of defect

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Recall Handling

"Inform the Department of Health?"

WHEN YOU NEED TO BE SURE SGS

Recall Handling

A recall…

"decision made by a company to call back a product batch that has been put on the market"

Definition by ISO 22716:2007

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Recall Handling

Some recalls are not quality or safety related… examples?

- Withdrawal – e.g. marketing strategy
- Voluntary
- Mandatory – Directed by the national regulatory authorities

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Recall Handling

- Involves removing or withdrawing a particular cosmetic product from all links of distribution
- Reasons can be:
  - Critical quality defects discovered
  - Serious adverse cosmetic reactions
  - Potential risks to users' health
- Authorized personnel should coordinate the recall process
- Initiation should be prompt and timely

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Recall Handling

- Inform and notify appropriate authorities if recalls initiated due to potential impact on consumer safety
- Safety alert – do the followings:
  - Advice regarding a specific situation of a product not conforming with safety specification
  - Disseminate the safety alert through mass communication media

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Recall Handling

Reasons for Recall

- Customer complaint
- Detection of GMP failure after release
- Result from the ongoing stability testing
- Request by the national authorities
- Result of an inspection
- Known counterfeiting or tampering
- Adverse reaction reporting

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Recall Handling

Designated Responsible Recall Person

- May be authorized person
- If not, must advise authorized person of results
- Sufficient support staff for urgency of recall
- Independent of sales and marketing
- Access to records

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Recall Handling

SOP for Recall

- Established, authorized
- Actions to be taken
- Regularly checked and updated
- Capable of rapid operation to hospital and pharmacy level
- Communication concept to national authorities and internationally

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Recall Handling

Distribution Records

- Avaliable to designated person for recall purposes
- Accurate
- Include information on:
  - Wholesalers
  - Direct customers
  - Batch numbers
  - Quantities

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Recall Handling

- **Written progress report and reconciliation**
  - Record progress as procedure followed
  - Reconcile delivered with recovered products
  - Issue final report
- **Effectiveness of procedures checked**
  - Test effectiveness from time to time
- **Secure segregated storage of returned goods**
  - Essential to keep returned goods away from other goods

Contract Production and Analysis

WHEN YOU NEED TO BE SURE

Contract Production and Analysis

Objectives

- To review general issues
- To understand the responsibilities of:
  - Contract giver
  - Contract accepter
- To understand the contract

Contract Production and Analysis

Principle

- Contract production and analysis must:
  - Be correctly defined, agreed, controlled in order to avoid misunderstandings that could result in inferior product
  - Have a written contract clearly establishing each parties' duties which ...
  - Clearly state how the authorized person when exercising his or her full responsibility releases each batch or issues certificate of analysis

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Contract Production and Analysis

General Issues

- Written contract must cover manufacture, analysis and any technical arrangements
- Should allow audit of contract acceptor
- In case of contract analysis, the authorized person must still given final release for sale

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Contract Production and Analysis

Responsibilities of the Contract Giver

- Must assess competence and compliance of contract accepter with GMP
- All necessary information must be provided to the contract accepter in order to:
  - Have the operations carried out correctly in accordance with the manufacturing authorization and other legal requirements
  - Be fully aware of any problems with the product, work, tests that might pose a hazard to premises, equipment, personnel, other materials or other products
- Authorized person
- Batch release in compliance with specifications

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Contract Production and Analysis

Responsibilities of the Contract Acceptor I

- Competence
  - Must have the necessary facilities, premises and equipment, both in type and in quantity, to undertake the work
  - Must have a manufacturing authorization to do this type of work
  - Its staff must have the necessary qualifications, training and experience to be able to do the work

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Contract Production and Analysis

Responsibilities of the Contract Acceptor II

- No subcontracting without approval
  - To accept a 3rd party, contract giver must be able to undertake audits needed to be reassured that the 3rd party is competent.
  - All the responsibilities placed upon the contract accepter must be fulfilled by any third party contractor that may be employed.
- No conflicting activities

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Contract Production and Analysis

The Contract – I

- Each party's responsibilities defined
- Technical aspects drawn up by competent persons
- Batch release mechanisms; by the authorized person
- Materials purchasing, testing and releasing
- Production and in-process QC (IPQC) and QC
- Sampling and analysis;
  - Who takes the sample?
  - And where?

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Contract Production and Analysis

The Contract – II

- Reference standards and retention samples
  - Who keeps them?
  - Where and under what conditions are they stored?
- Records:
  - Manufacturing
  - Analysis
  - Distribution

  should be kept by or made available to contract giver
- Rejection management needs to be described for:
  - Starting materials
  - Intermediate and bulk product
  - Finished product

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Contract Production and Analysis

Possible Issues – I

- Owners insist on using unsuitable facilities
- Owners insist on using relatives' facilities
- No time to validate new facilities
- Contract accepter takes on inappropriate new product

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Contract Production and Analysis

Possible Issues – II

- Contract accepter does not have all specified equipment
- Contract accepter uses incorrect equipment
- Contract accepter does not follow agreed procedures

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Contract Production and Analysis

Possible Issues – III

- Contract accepter uses an alternative material supplier
- Contract accepter working with out-of-date specifications

Internal & External Audits

"2 weeks of sleepless nights and I still failed the inspection! Why is this happening to me?"

WHEN YOU NEED TO BE SURE

Internal & External Audits

Audits

"*… a tool which is designed to monitor the implementation and the status of these cosmetic GMPs and, if necessary, to propose corrective actions.*"

ISO 22716:2007 – 16.1

Internal & External Audits

Objectives

- To identify the role of self-inspection in the quality management system
- To review the way in which a self-inspection programme should be carried out
- To discuss what to check in a company's self-inspection

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Internal & External Audits

Audits

- Conducted by designated competent personnel
- Independent and detailed
- Resist attempts to influence decisions
- All observations made → evaluated and shared with appropriate management
- Follow-up → confirm satisfactory completion or implementation of corrective action

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Internal & External Audits

Some tips…

The auditor must…

- Be able to present factual report
- Have a good working knowledge of the legislation & GMP guidelines
- Be able to offer assistance, in his or her opinion, to serve the public interest.
- Be able to motivate a manufacturer to comply with GMP or correct specific deficiencies
- Resist attempts to influence decisions

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Internal & External Audits

Some tips…

Communication skills…

- Use suitable language to the levels of the persons being addressed
- Body language – gesture
- Show interest by encouraging with a smile and a nod of the head
- Keep your arms open, not crossed
- Be aware and sensitive to the prevailing company culture
- Be diplomatic

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Internal & External Audits

Principle – I

- Ensures that a company's operations remain compliant with GMP
- Assists in ensuring continuous quality improvement
- Should
  - Cover all aspects of production and quality control
  - Be designed to detect shortcomings in the implementation of GMP
- Must
  - Recommend corrective action if shortcomings are observed
  - Set a timetable for corrective action to be completed

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Internal & External Audits

Principle – II

Special occasions may demand additional self-inspections. For example

- Recalls
- Repeated rejections
- GMP inspections announced by the National Authorities

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Internal & External Audits

Principle – III

- Team consist of personnel who can evaluate the situation objectively
- No conflict of interest
- No revenge in mind
- Should have experience as observers of a self-inspection team before becoming team member
- Lead self-inspector with experience as team member

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Implementing ISO 22716

- **Internal audits (16).**
  - The organization of Internal Audits (to Self Inspect the internal organization) is a requirement for Cosmetics manufacturing organizations. Each department in the organization has to undergo the internal audits, on a frequent and scheduled basis. The quality unit needs to organize and also needs to appoint the auditors, to ensure competency and independency of personnel. Internal audits have to be followed up by preparing Corrective Action listings and the aim for Continuous Improvement should be clearly visible (e.g. resulting in an effective CAPA program).

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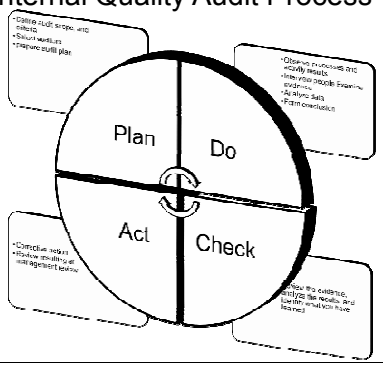
Internal Quality Audit Process



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Internal & External Audits

Scope of Self-Inspection Programme – I

- Written instructions
- Covering all aspects of GMP:
  - Personnel
  - Premises including personnel facilities
  - Maintenance of buildings and equipment
  - Storage of starting materials and finished products
  - Equipment
  - Production and in-process controls
  - Quality control

Internal & External Audits

Scope of Self-Inspection Programme – II

- Documentation
- Sanitation and hygiene
- Validation and revalidation programmes
- Calibration of instruments or measurement systems
- Recall procedures
- Complaints management
- Labels control
- Results of previous self-inspections and any corrective steps taken

Internal & External Audits

The Self-Inspection Team

- Team leader needs:
  - Authority
  - Experience
  - May be appointed from inside or outside the company
- Team members, including:
  - Local staff who are familiar with the area
  - Experts in their own field
  - Familiar with GMP
  - May be appointed from inside or outside the company

Internal & External Audits

Carrying Out a Self-Inspection

- Frequency
  - May depend on company requirements and the size of the company
- Report:
  - Results
  - Evaluation
  - Conclusions
  - Recommended corrective measures, if applicable
- Follow-up action
  - Company management must evaluate both the report and corrective actions

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Internal & External Audits

Pre-inspection

- Organize the team with a leader who will
  - Plan the inspection
  - Lead the opening and exit meetings
  - Prepare the deficiency and final report
- Inspection reviews
  - Manufacturing license
  - Site information file
- Prepares an audit plan & checklist

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Internal & External Audits

The Inspection

- Opening – introductions
- Brief discussion on the purpose of the visit and gather updates from the company to plant operations
- Presents audit plan

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Internal & External Audits

The Inspection

- Perusal of documents:
  - Layout of site
  - Diagrams of utilities
  - Self inspection / internal audit reports
  - Complaints file
  - SOPs
- Plant tour
- Interview of personnel
- Team meets to discuss & prepare deficiency report
- Exit meeting – audit outcome & discussion may be held

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Internal & External Audits

Classification of Findings

- Major
  - Minimum risk that finished products may not meet performance requirements or specifications.
- Minor
  - No risk that product will not meet performance requirements or specifications.
- Opportunity for Improvement

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Internal & External Audits

Supplier Audits

- QC department should have responsibility together with other relevant departments for approving suppliers
- Ensures suppliers can reliably supply materials that meet established specifications
- Avoids trying to test in quality to goods received from dubious sources
- Before suppliers are approved they should be evaluated
- Should take into account the supplier's history and nature of materials to be supplied.

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Internal & External Audits

Auditing the Self-Inspection Programme – tips I

- GMP inspector should assess:
  - The SOP
  - Programmes
  - Checklists or “aide memoire”

Internal & External Audits

Auditing the Self-Inspection Programme – tips II

- The SOP should describe teams, process, and frequency of self inspection
- Company policy may not permit GMP inspector to see actual deficiency reports and corrective actions
- GMP Inspectors should be looking for compliance with the self-inspection SOP – not necessarily at actual deficiencies recorded
- Seek objective evidence of reports and action

Internal & External Audits

Auditing the Self-Inspection Programme – tips III

- Ensure company is not just doing housekeeping or safety audits

GMP (Good Manufacturing Practice) for Cosmetic Products

End of Section 6

WHEN YOU NEED TO BE SURE SGS