Good Manufacturing Practice Considerations

Ben Elmadi - Technical Manager
MSL Solution Providers

GMP - ISO 22716 Principles

15 Clauses

- Clause 3: Personnel
- Clause 4: Premises
- Clause S: Equipment
- Clause 6: Raw materials and Packaging
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Aims of today

- Provide you a basic understanding of GMP and microbiology in manufacturing
- Explain the risks and potential outcomes
- Explain how GMP should help manufacturers

What is GMP?

A system for managing critical manufacturing processes and controls to ensure consistent product quality.

Key guidance principles:

- ISO 22716:2007 (required in the EU)
- HACCP (Food industry)
- Covers all aspects of manufacturing (QMS to practical)

It is all about risk analysis

GMP Certification

Is there a mandate for certification:

In short – **No.**

Manufacturers can self certify / claim they conform to ISO 22716 principles

External certification is typically pushed by buyers and brands.

External certification provides reassurance that an impartial 3rd party has reviewed evidence of ISO 22716 principles being followed.

GMP - ISO 22716
Principles

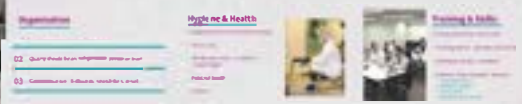
15 Clauses

Clause 3: Personnel

Different challenges based on company size

Principle

The personnel involved in the manufacturing site should have adequate training, instructions and controls.



Principle

The personnel involved in the manufacturing site should have adequate training, instructions and controls.

Organisation

01 Organisation chart - Clear structure

02 Quality should be an independant person or team

03 Communication - Billboards, newsletters, email

Hygiene & Health

A policy should be in place that covers:

- Dress code
- Designated areas - controlled / uncontrolled
- Personal health
- Visitors

Training & Skills

Training should be monitored:

- Training matrix - provides an overview
- Individual record - Evidence
- Defined review periods / reasons
  - Long absent leave
  - Change to process
  - Every 2 years
  - Should be based on risk

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Clause 4: Premises

Important for everyone, not usually an issue

Principle

The site should be fit for the purpose of the activities required

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Set up

01 Area types should be clearly defined

02 Design of infrastucture should not encourage contamination

03 Adequate facilities should be present e g , washing

Cleaning

Tidy site a tidy mind.

Clutter leads to mistakes and long root cause investigations

Cleaning activity should be logged

Pest Control

Different sites [illegible] many forms.

All sites should have adequate pest control measures in place

The exterior of the premises should be taken into consideration e does the surrounding area invite pests

Set up

01 Area types should be clearly defined

02 Design of infrastucture should not encourage contamination

03 Adequate facilities should be present e.g., washing

Cleaning

Tidy site a tidy mind.

Clutter leads to mistakes and long root cause investigations

Different areas have different risks

Cleaning activity should be logged

Pest Control

Different sites will have different risks, pests come in many forms:

- Insects
- Rodents
- Birds

All sites should have adequate pest control measures in place.

The exterior of the premises should be taken into consideration i.e., does the surrounding area invite pests.

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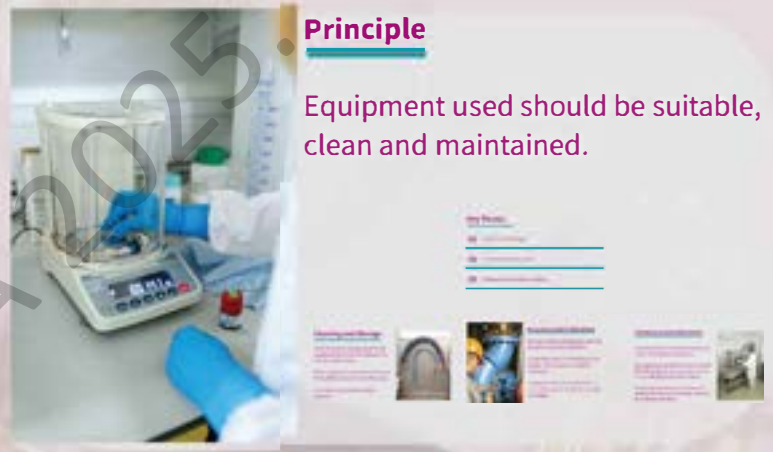
Clause 4: Equipment

Always important and will likely negatively impact smaller manufacturers more due to costs implications



Principle

Equipment used should be suitable, clean and maintained.

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Key Points

01 Cleaning and storage

02 Accuracy and calibration

03 Maintenance and authorisation

Cleaning and Storage

There should be storage space for all equipment that does not increase the risk of conta mination.

When equipment is cleaned with water, it should be allowed to dry effectively.

Air drying is typically the safest approach.

Accuracy and Calibration

Accuracy checks are typically done at the start or during production.

Equipment used to manufacture and quality check product should be calibrated

If equipment is out of calibration a non-conformance should be raised to investigate

Maintenence and Authorisation

Sites should have an equipment log and a form of tracking maintenance.

Equipment not suitable for use should be identified clearly e.g., removing from an area or labelling equipment clearly.

Personnel authorised to operate and change the status of equipment should be available and clear

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Clause 7: Production

Principle

Each operation should be adequately monitored

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Documented Processes

Traceability and Controls

Storage of product

Key Points

01 All processes should be documented

02 All key actions should be recorded

03 The shelf life starts at the blend completion date

Documented Processes

All blends made on site should have a defined formula and blend process

All blending and filling operations should include start up checks before commencing.

All staff should be trained in the operations they are performing.

Traceability and Controls

Batch numbers should be assigned to each product made (most sites will have a blending order number and then a separate filling order number for full traceability).

All in process controls should be defined and risk based.

Examples of in process controls: weight, temperature, pH, labelling / stamp legibility, bottle top torque.

Key process actions should be signed at the time of completion.

If its not recorded, it didn't happen!

Storage of product

Similar principles to raw materials.

Partially used IBC's should be risk assessed.

Status, and identification system should be in place for all products.

Shelf life should be considered i.e., the product expiry starts from blend completion not filling.

Key Points

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Clause 8-10: Finished Product, QC Laboratory & Out of Specification

Principle

Finished product should meet a defined acceptance criteria.

The QC lab is responsible for all controls being monitored

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The QC lab is responsible for all controls being monitored.

Sampling and Release

Shipment and returns

Typically sites will operate on a FIFO system, this is best practice.

All shipments and returns should be recorded for quality assurance.

Any returned product should have a documented re-evaluation before it can be released to the market again.

Out of specification

Non-conformances and investigations should be documented.

Retesting should be done with justification (no testing until a favourable result).

Product in may be reprocessed providing a rationale is documented.

Only authorised personnel (should be defined in SOP) can sign off investigation outcomes.

Sampling and Release

All products must meet their defined specifications.

Each product batch should be tested for bioburden and compared against the acceptance criteria defined in ISO 17516. Where testing is not performed, a documented risk assessment must be available.

ISO 29621 provides guidance for risk-based approaches.

Only authorised personnel (typically the Quality team) may approve product release.

Sampling frequency should be risk based and documented.

Retain samples should be adequately stored for the shelf life of the product

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Clause 11-13: Waste, Sub-contract & Deviation

Principle

Waste should be disposed of appropriately, agreements with suppliers are clear and deviations in services are reviewed sufficiently.

Waste

Sites should have a segregated waste area.

Waste should be organised and stored based on hazards e.g., oxidisers should be stored separately from flammable substances.

Contracts with waste management, where appropriate, should be available at all times.

Subcontractor Deviation

Non-conformances and investigations should be documented.

Preventive actions should be in place to avoid recurrence.

Subcontracting

Very similar to ISO 9001 principles.

Service provider ability should be assessed before approval.

It may be necessary to audit the service provider at a defined frequency (if they provide a key service).

A contract with clear responsibilities should be in place.

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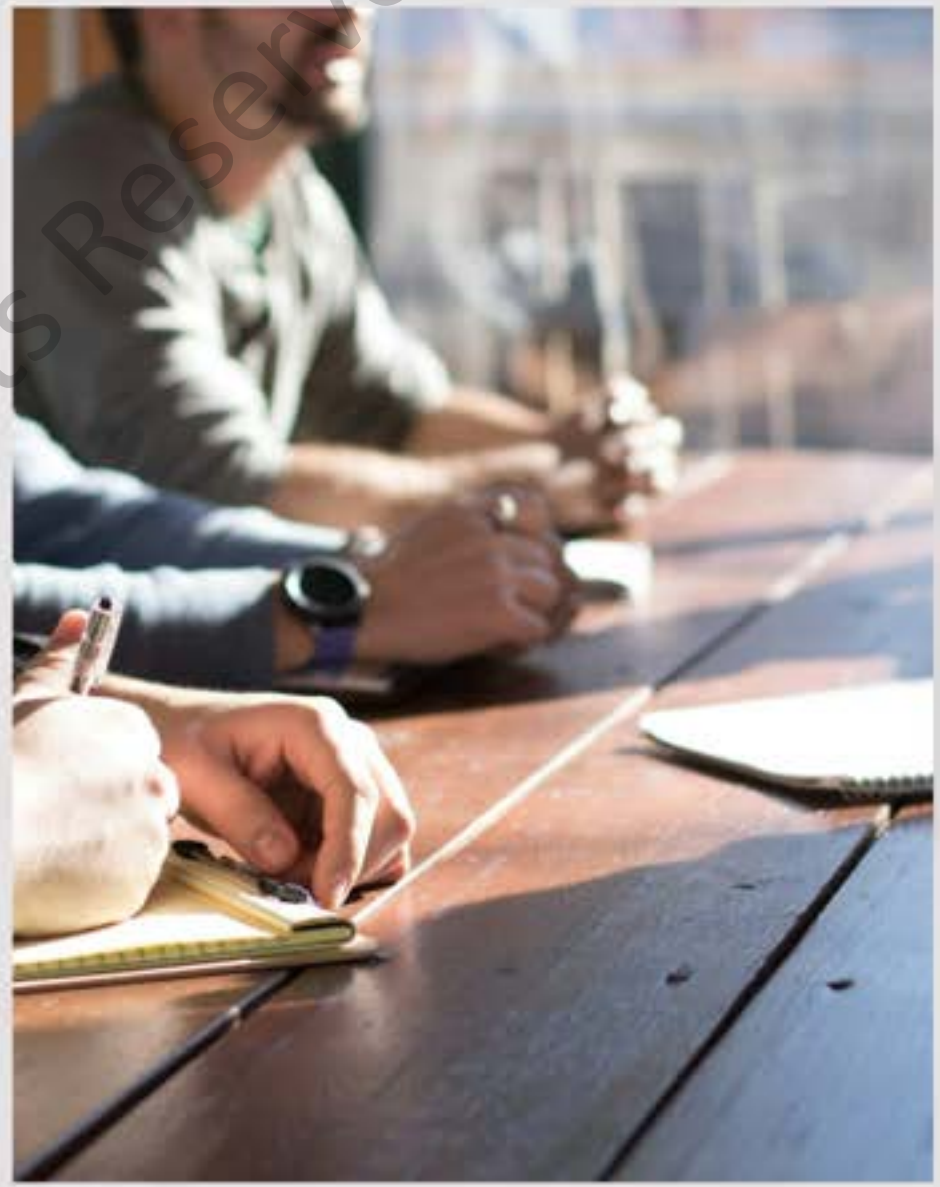

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Clause 14: Complaints and Recall

Often lacking in smaller manufacturers

Principle

All complaints are investigated and actioned

The site is recall ready

Complaints

"We never get complaints"
or
"We don't monitor or record complaints"?

This will likely be exposed when reviewing clause 10: internal audits.

A complaint log should be in place for trending.

Key complaint information should be recorded: reason, root cause, corrective and preventative action and effectiveness.

Product Recalls

A recall procedure should be in place with clearly defined rolls.

Product recall procedures should facilitate a timely roll out.

Hopefully no real recalls occur, if so, mock recalls should be conducted.

Any recalls (mock or real) should be evaluated for effectiveness and improvement actions raised.

Complaints

"We never get complaints"
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Clause 15: Change Control

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Principle

Changes that impact the quality of a product or a process should be approved and implemented by competent and authorised personnel.

A recent deodorant recall was reported to have a change control failure as the root cause.

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Clause 16: Internal Audit

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Principle

Internal operations and controls may be written but are they being implemented effectively.

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Approach

Managed by the quality team (independent of the area being audited).

A schedule should be established and followed.

All observations should be evaluated and shared with appropriate management.

All actions raised and implemented should be followed up for effectiveness.

A Personal Lesson

It is not good practice for audits to point fingers at people, it should identify problematic processes and systems.

The answer is not to add more paperwork for traceability. It is often to make the process more relevant and appropriate.

This clause is important to demonstrate all other clauses are being followed throughout the year.

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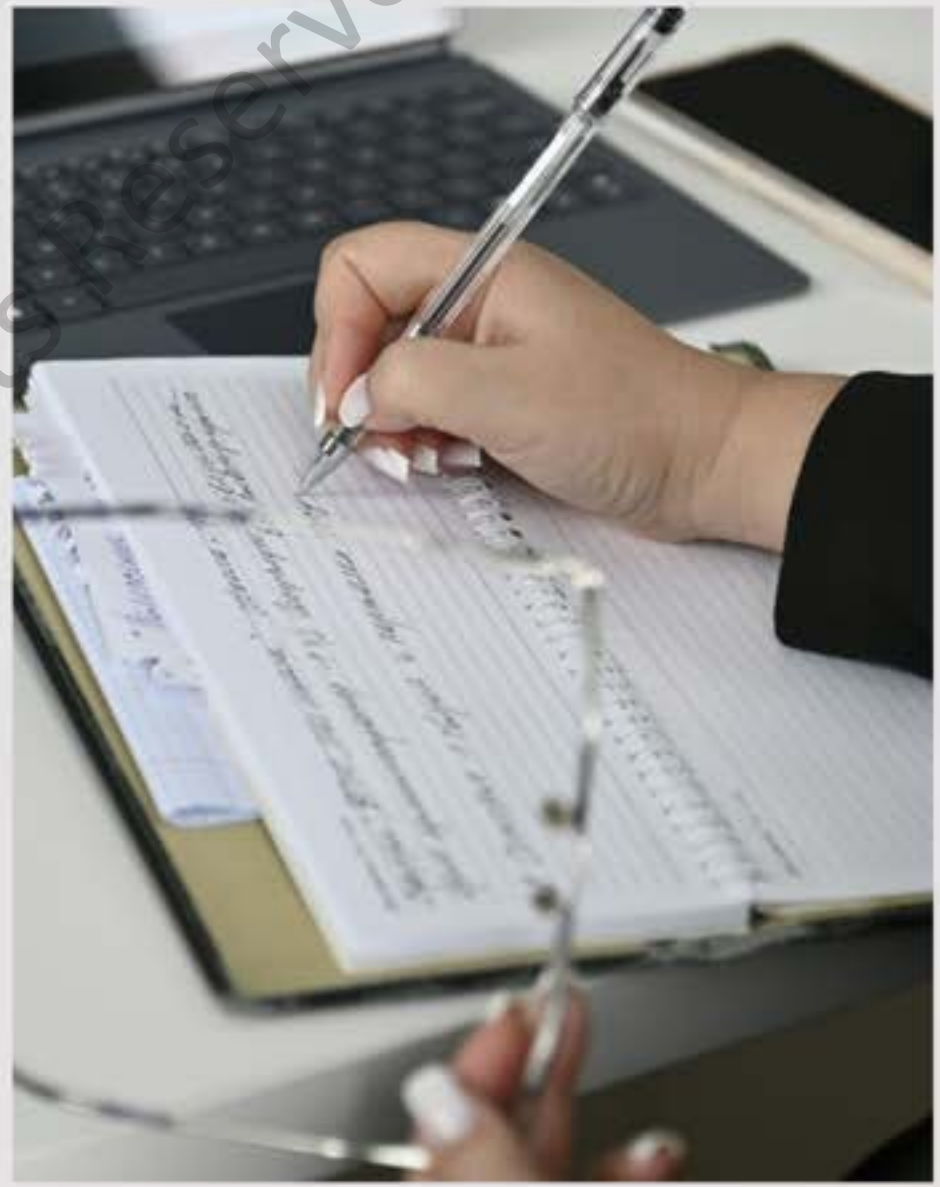

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Clause 6: Raw materials and Packaging

3 key risk areas for microbiological control

Principle

All raw materials on site should meet a **defined** acceptance criteria

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Purchasing and Receipt

Status and Release

Storage and re-evaluation

Water Quality

Key Points

01 Raw materials bought should be assessed for quality

02 Storage will impact the true shelf life of a raw material

03 Water quality is extremely important

Water Quality Cont.

Purchasing and Receipt

Manufacturers must maintain an approved supplier list.

Incoming materials should be inspected for integrity at the point of receipt — this may include laboratory tests (e.g. pH).

Written procedures must be in place to cover these activities.

The Certificate of Analysis (CoA) should be verified and documented.

Status and Release

A procedure should be in place that allows clear identification of raw material status e.g., quarantine (yellow sticker), approved (green sticker).

Only authorised persons should be able to change the status of a raw material.

Key information should be captured on the label of all materials on site including: Name, product code, batch reference, and expiry.

Storage and re-evaluation

Storage conditions should be appropriate for the raw material e.g., hygroscopic powder shouldn't be stored in a humid environment.

Packaging should be closed when not being used: IBC caps and lids secure.

An SOP for product re-evaluation should be in place and authorised personnel clearly defined for sign off.

Water Quality

ISO 22716 is rather vague, but this is a critical control point.

It is the most expensive problem to fix.

It is the most overlooked raw material.

It is the most common raw material.

Major root cause of contamination problems!

Water Quality Cont.

The standard requires:

- Water quality be defined
- Water quality be tested and monitored
- Water systems be set up to avoid stagnation

Adequate risk assessing would require water quality include microbiological.

There is no universally accepted process water quality.

Sites should conduct their own risk assessment.

Home manufacturers should be boiling water before using.

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Often lacking in smaller manufacturers

Principle

Documentation is a core principle of all quality systems. Therefore it must be organised and managed effectively.

All documents should have a unique reference.

All controlled documentation e.g., SOP's should be security controlled to prevent accidental change.

All documentation should be approved by appropriate personnel before being distributed.

Documents should be effectively archived when obselete and the length of storage should be defined.

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Key Takeaways

You are a fresh pair of eyes for manufacturers.

You will see risks they don't, all decisions should be risk based.

GMP is not policing, it is improving.

Having a pragmatic / collaborative approach leads to success.

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