Quality Guide for Supplier of YPSOMED AG

Quality Control, Ypsomed AG
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Foreword

Ypsomed AG is a company that has particularly specialised in the development and manufacture of injection pens and pen needles.

Since Ypsomed operates in a medical equipment environment and cultivates partnerships with numerous successful pharmaceutical and biotech companies, the Company is subject to strict legal requirements that serve to protect product users. In order to meet these requirements Ypsomed follows the principles of Good Manufacturing Practice (GMP) and is certified in accordance with QM standards ISO 9001 and ISO 13485.

This Quality Guide is designed to enable suppliers with little practical experience in the field of medical equipment to address issues in this industry and provide them with assistance in satisfying the relevant requirements.

By way of supplementing any contractual agreements, the Quality Guide for suppliers contains the following:

- Abridged instructions and detailed descriptions of particularly complex subject areas
- Assistance in the form of forms / reports filled in by way of example
- Ypsomed's expectations regarding hygiene, cleanliness, documentation practice to be applied as well as audit rights

Contents

1 Quality and legal requirements in the medical device sector

1.1 Quality

In addition to fulfilment of specified requirements, the term **medical device quality** implies that it is suitable for the intended use. This means that:

- the intended function is guaranteed throughout the entire service life.
- the labelling and instructions for use are correct.
- there is no quality deterioration as a result of storage or transport.
- the device is safe for patients, users and third parties.
- any risk emanating from the device is minimised and acceptable in relation to the benefit.

The quality of medical devices is regulated by law and is subject to continuous monitoring because:

- it can have a direct impact on people's health.
- the patient cannot reliably detect any hidden defects.
- the law aims to protect the safety of patients.

The quality of the device **and** documentation must be guaranteed!

- A good-quality device meets the requirements of customers.
- Seamless documentation makes it possible to produce evidence of device quality at any time.

1.2 Legal requirements / GMP

Due to the strict regulatory requirements to which Ypsomed is subject it is absolutely essential that all the legal requirements be met. Evidence of conformity with these legal requirements can be produced by applying and observing relevant standards that are regarded as international state of the art and by applying the principles of Good Manufacturing Practice (GMP).

2 Documentation requirements

In order to meet the GMP requirements, basic rules for correct documentation must be observed. For this reason the following documentation principles shall apply:

- Permanent — The information cannot be changed, deleted or removed.
- Legible — The entry is readily legible.
- Careful — Calculations are correct and the entries contain no errors.
- Immediate — The recording is performed by the operative during or directly after the relevant activity and never beforehand.
- Unambiguous — An entry has the same meaning for every reader.
- Congruous — The various entries and records are devoid of incongruities.
- Complete — All the required information is present and in the event of corrections, reasons are stated.
- Direct — Data is documented directly on the record provided.
- Truthful — The records reflect the true facts and are made according to the best of the recorder's knowledge and belief.

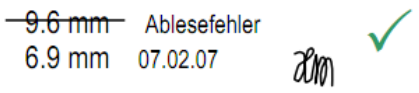
Note: What has not been written down has not taken place!

Documentation guidelines – notes

The use of correction aids such as fluids (Tipp-Ex), correction tape, correction pens or the like is not allowed.

If an entry has to be corrected, it is **crossed out horizontally** and initialled and dated so that it continues to be **legible**. The correct entry is added in writing. If the reason for the correction is not apparent, a plausible reason must be given in addition.

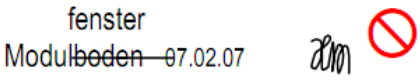
- Right correction



- Wrong correction

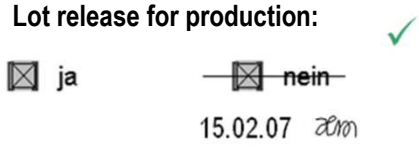
Partial corrections are not allowed because the correction area has to be marked very accurately so that it is absolutely clear. This also applies to the date.

- Wrong correction



Boxes where a cross has been placed by mistake are crossed out horizontally.

- Right correction



Quality-relevant documents must be authorised by applying the date / signature or date / initials.

3 Line Clearance

The reason for Line Clearance is the aim to avoid batches being mixed and ensure seamless traceability.

Line Clearance is the process of removing from the workplace all products previously manufactured, documents used, equipment used and all other materials that will no longer be used for the next series being processed. For certain processing steps it may be necessary to perform additional cleaning or decontamination of the work surface and equipment.

Line Clearance – notes	
	What has to be performed (checked)?
	No materials from the last order!
	No unnecessary equipment from the last order!
	No documents, labels, forms, etc. from the last order!
	Machine or workplace cleaned!
	IMPORTANT: Check and document!

Line Clearance must be checked and documented. The best and most reliable way of documenting results is on the working documents.

4 Processing complaints / defect notices

4.1 Principles

- Complaints can be a tool for ensuring the success of a company.
- Complaints must always be processed immediately. For the customer it is very unpleasant not to get any response to a complaint.
- For the processing of complaints it is necessary to have personnel with excellent training.
- Complaints must be processed according to the best of the person's knowledge and belief (honest description of the situation, professional analysis of the cause(s), suitable corrective action).
- Keep in touch with the customer, e.g. ask about the next batch delivered and whether the measures for improvement have been successful.

4.2 Documentation

The 8D report is a suitable means of documenting the causes and measures taken in the event of a complaint.

The 8D problem-solving method originates from the automotive industry and supports the processing of a complaint by taking a systematic approach. '8D' refers to 8 disciplines or 8 steps that have to be completed successively and documented in a verifiable manner.

Discipline	Keyword	Explanation
1	Problem-solving team	■ Who is going to look after it? ■ Teamwork to identify a solution!
2	Problem description	■ Where is the problem? ■ Is it a repeat deviation? ■ What do I want to achieve (objective)?
3	Define immediate action	■ What has to be accomplished immediately to ensure that the deviation can be ruled out on the next batch?
4	Root cause analysis	■ What is the cause? ■ Why was it not detected?
5	Plan corrective action	■ How can the deviation be avoided in future? ■ Effective measures for improvement! ■ The training of employees is not usually a measure because the problem often has to be sought in events!
6	Implementation of measures	■ Does it have to be documented in full? ■ Qualification and validation?
7	Prevent error repetition	■ Are the measures useful and effective? ■ Have we achieved our objective?
8	Success monitoring and closure	■ Document success based on ensuing batches produced!

A template for an 8D report can be found in Annex 1.

5 Hygiene and cleanliness

5.1 General

Hygiene and cleanliness throughout the company are the basic prerequisites for being able to manufacture good-quality products.

5.2 Expectations

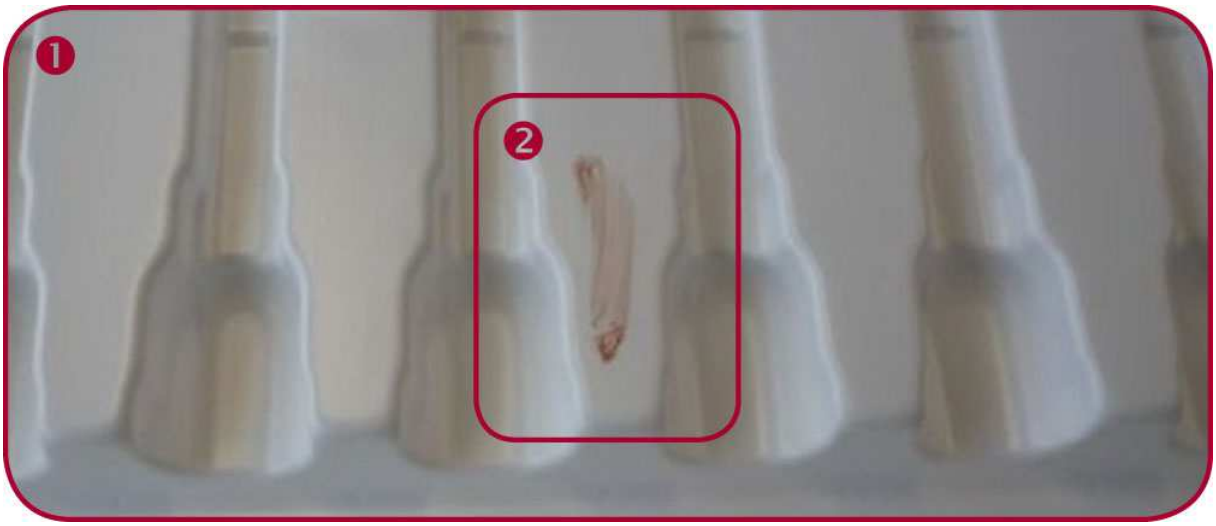
Absolute cleanliness is expected with regard to the product and packaging

- No grease, oil or other residues
- No foreign matter
- No hairs
- etc.

These expectations can be met by taking very simple measures (e.g. wearing working clothes that are changed regularly; wearing head caps; etc.).

5.3 Wounds

No customer wants to see anything like that!



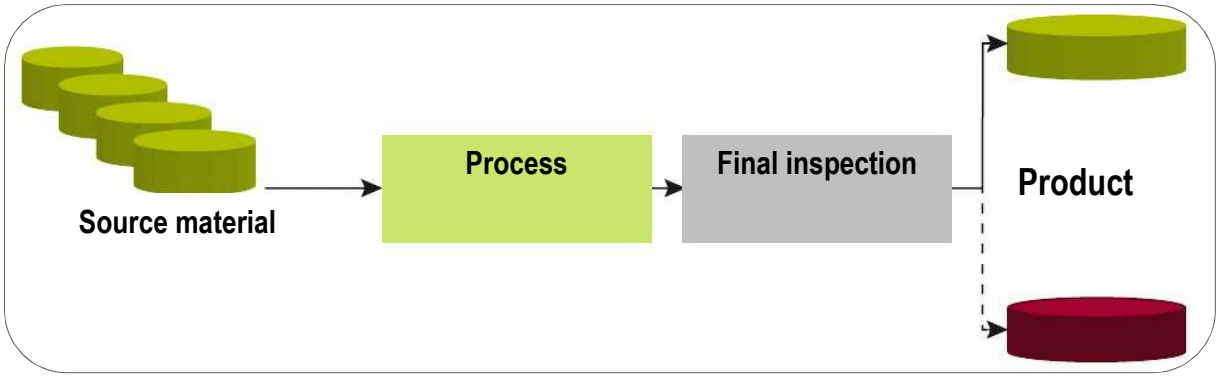
❶ Workpiece holder for finished components ❷ Dried blood

What has to be done in the event of injuries / wounds?		
1	Interrupt work immediately	
2	Wound treatment	Disinfect the wound and cover it with a waterproof dressing
3	Workplace	Clean the workplace and disinfect it if necessary
4	Superior	Notify your superior
5	Dispose of material	Segregate contaminated material and dispose of it
6	Change of workplace	The employee involved may have to temporarily change his or her workplace.
7	Documentation	The incident must be documented.

6 Process validation / equipment qualification

There are requirements in the valid QM standards stipulating that all processes for manufacturing products and rendering services must be validated unless the results thereof can be verified with the following inspections (100% control).

Why validate?



6.1 Definitions

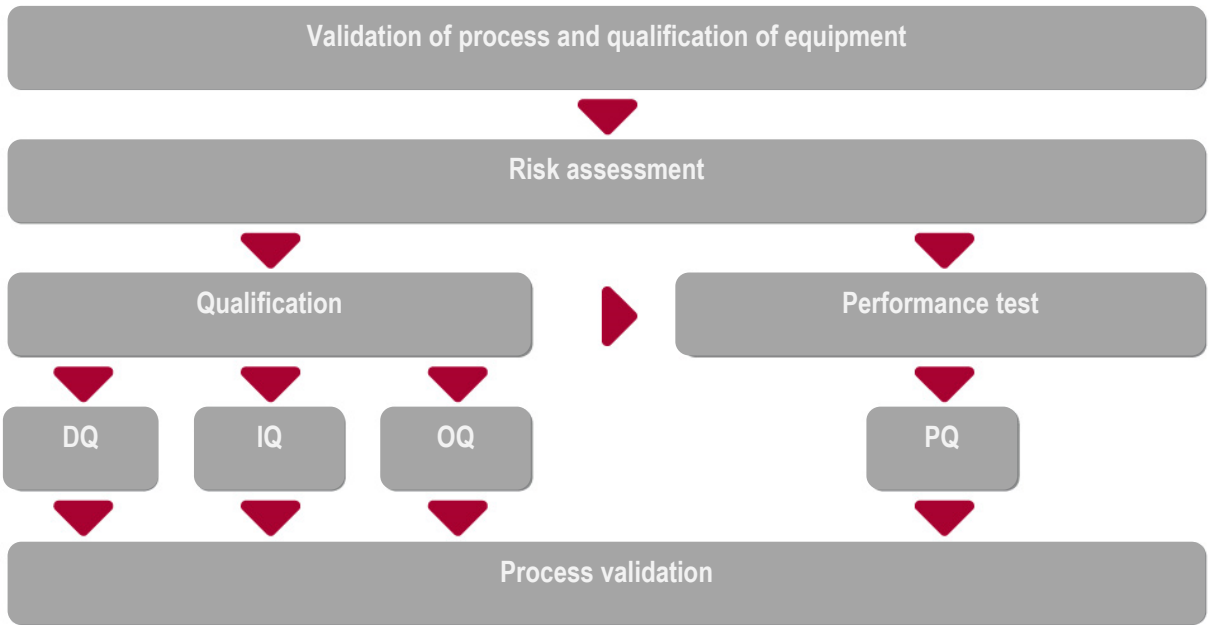
Qualification

- It is **system- / equipment-related.**
- It constitutes evidence of the suitability of rooms, systems and equipment.

Validation

- It is **process-related.**
- It constitutes evidence that with a high degree of reliability a certain manufacturing process continuously produces a product that meets predefined specifications and quality criteria.

6.2 Sequence / overview



6.2.1 Design Qualification DQ

A Design Qualification represents the interface between the User Requirement Specification on the one hand and the Performance Specification (part of the contract) on the other. A DQ documents the fact that all the standards and directives applicable to the machine or system, all the GMP rules, all the specifications also applicable within the company, and especially all the requirements contained in the User Requirement Specification have been incorporated and implemented in the planning of the machine or system.

6.2.2 Installation Qualification IQ

An Installation Qualification includes the acceptance test on the system by the supplier.

The following items must be taken into consideration in Installation Qualification:

- Sets of technical documentation
- Equipment list / maintenance (list of all the equipment used)
- Energy and media supply
- CE Declaration of Conformity / Manufacturer's Declaration
- Material of parts with product contact

6.2.3 Operational Qualification OQ

Before the OQ tests can be commenced it is absolutely essential to process all the critical defects resulting from Installation Qualification. That is the only way in which it is possible to ensure that the tests are performed on a machine or system that has been correctly installed.

An OQ is documentary evidence of the fact that equipment and systems are operating reliably within the defined limits.

The following items must be taken into consideration in Operational Qualification:

- Standard operating procedures
- Test equipment for qualification
- Verification of ambient conditions
- Operational test plan / release
- Testing of operator controls
- Testing of control software
- List and testing of error messages

6.2.4 Performance Qualification PQ

A PQ is documentary evidence of the fact that the qualified equipment and systems can be used to manufacture products of the specified quality.

The following items must be taken into consideration in Performance Qualification:

- Description of the performance required
- Description of the performance provided
- Result analysis of PQ

Details on system qualification and process validation incl. templates and examples can be found in Annexes 2-6.

7 Audit rights

Vendor which are classified “critical / crucial“ according to European Commission Recommendation 2013/473/EU (primarily vendor providing customized materials/products that are used for final products where Ypsomed is the legal manufacturer), shall grant Ypsomed, representatives of its notified body as well as the authorities responsible for Ypsomed's final product access to the facilities relating to the Ypsomed products.

The audits / inspections by representatives of Ypsomed's notified body can also be conducted unannounced. Respective vendor have notice of European Commission Recommendation 2013/473/EU, grant access to the facilities and documentation relating to the Ypsomed products at any time and assure an unannounced inspection.

8 Annex

[1] Template of an 8D report

[2] System qualification and process validation

[3] Example of a validation plan

[4] Template of an initial sample inspection report

[5] Example of qualification

[6] Measurement Systems Analysis MSA