Quality Guide for Suppliers YPSOMED AG

Quality Control, Ypsomed AG
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Foreword

Ypsomed is the leading developer and manufacturer of injection and infusion systems for self-medication and a proven diabetes specialist with over 35 years of experience. As an innovation and technology leader, it is the preferred partner of pharmaceutical and biotech companies for pens, auto-injectors and pump systems for the administration of liquid medications. Ypsomed presents and distributes its product portfolios under the umbrella brands mylife™ Diabetescare directly to patients or via pharmacies and clinics, and under YDS Ypsomed Delivery Systems in the business-to-business sector to pharmaceutical companies.

It is headquartered in Burgdorf, Switzerland, and has a global network of production sites, subsidiaries and distribution partners and employs around 2'000 people worldwide. As Ypsomed operates in the medical technology environment and maintains 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 guidelines of MDR (EU) 2017/745, the principles of Good Manufacturing Practice (GMP) and has a certified QM system according to ISO 13485.

This quality guide is intended to enable suppliers with little practice in the field of medical technology to deal with topics from this sector and to provide assistance in meeting the relevant requirements.

The Quality Guide for Suppliers contains additional information to any contractual agreements:

- 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

Inhalt

1 Quality and legal requirements in the medical sector

1.1 Quality

In addition to fulfillment the 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 or third parties.
- the 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 product **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).

1.3 Certificates

The content requirements are defined within the technical or purchasing specification and, if applicable, in the quality assurance agreement (QAA). A COC or COA is usually required. The content and structure of the document is based on DIN EN 10204:2005-01. In principle, the following information must be shown on the certificate as a minimum:

- Quantity details
- Reference to order / order number
- Batch number (supplier)
- Date of manufacture

Over-deliveries (physical delivery quantity in relation to the certified goods) are generally to be regarded as more critical than under-deliveries, as these would involve non-inspected goods. Such events prevent acceptance / use of the goods by Ypsomed.

1.4 Labelling

The content requirements are defined within the technical or purchasing specification and, if applicable, in the quality assurance agreement (QAA).

In principle, the following information must be shown on the label as a minimum:

- Order number
- Article number
- Batch number
- Quantity

The labelling must be visible on each container / outer carton. Double labelling is obligatory for cleanroom goods (double packaging).

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.

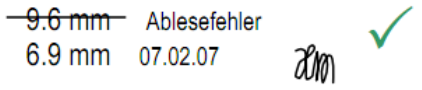
Note: What has not been written down has not taken place!

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 initialed 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



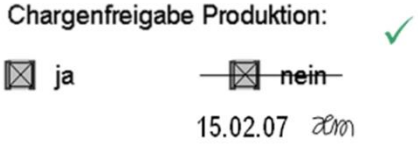
- Wrong correction

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 or as digital proof in the ERP system. In this case, the proof must be ensured via an individual employee login (code, badge,...).

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. => first response within 24h; 3D within max. 72 hours, or as defined in existing contracts.
- 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.
- In the case of return deliveries, e.g. for sorting / reworking, this must be made via a return delivery order. Re-deliveries must be made via a new purchase order. If reworks or supplementary processes are used on a batch that has already been delivered, this must be recognizable, e.g. by a new batch number or a numerical addition (e.g. _1; #1,..).
- Transport damage - responsibility / liability according to delivery agreements INCO-Terms

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 it was not detected?
5	Plan remedial 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! Control of success / proof of effectiveness

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 for environmental conditions

Absolute cleanliness is expected with regard to the product and packaging. The specification is made in technical or purchasing specification.

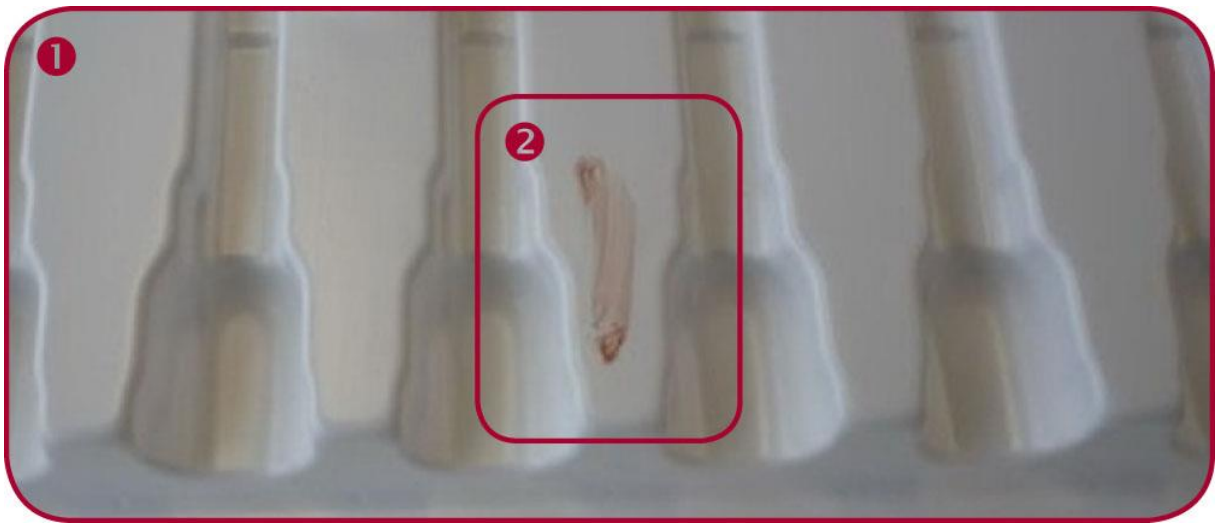
If manufacturing or packaging under controlled conditions / environments or in a clean room is defined, it is expected that a continuous zone and clothing concept is established and a pest control is implemented, monitored and evaluated.

- 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!



1 Workpiece holder for finished components 2 Dried blood

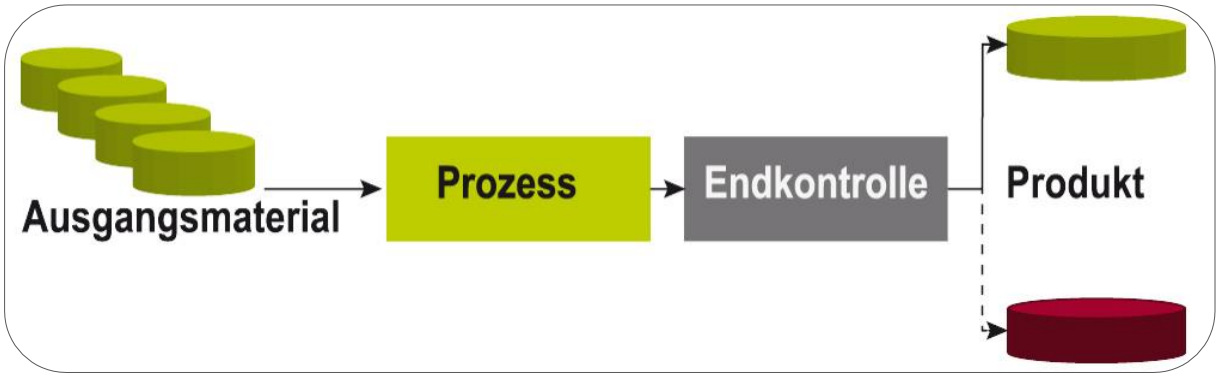
What has to be done in the event of injuries / wounds?		
1	Interrupt work immediately	
2	Wound treatment	Disinfect the wound and cover it with a waterproof dressing
3	Workplace	Clean the workplace and disinfect it if necessary
4	Superior	Notify your superior

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 to validate?



6.1 Definitions

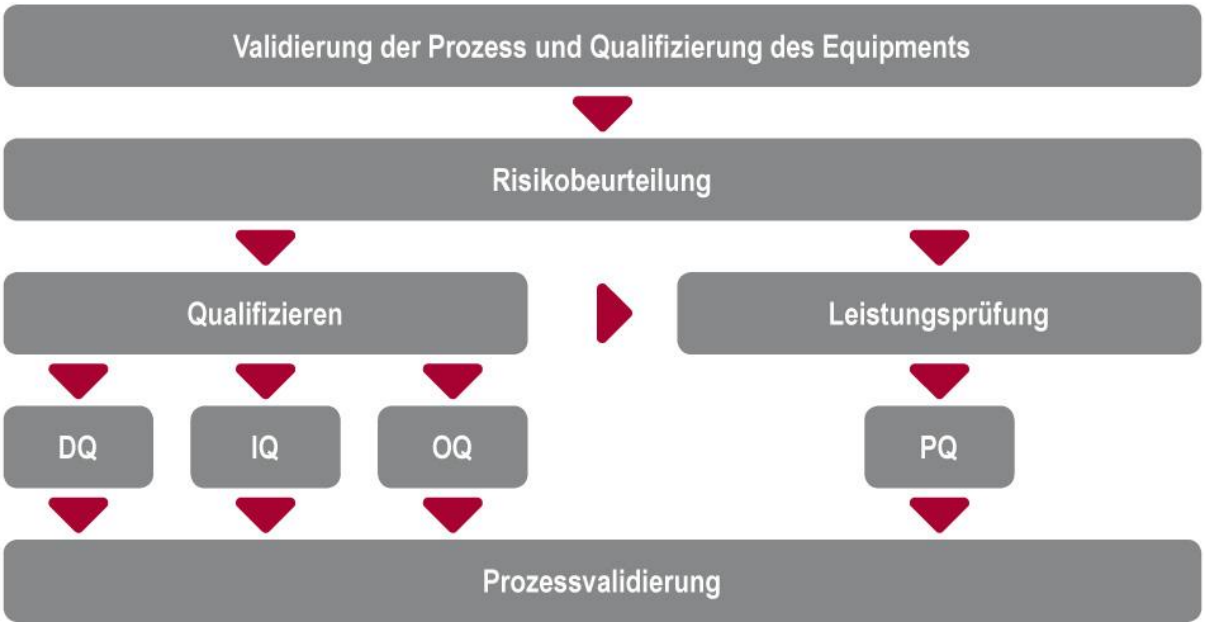
Qualification

- It is system-related
- It constitutes evidence of the suitability of rooms, systems and requirement.

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

The installation qualification includes the acceptance of the equipment by the supplier. If the equipment used has already been used for other validations, parts of it can be used for the IQ.

If a new plant/equipment or operating equipment is used, the performance of an initial IQ is mandatory. The following points must be taken into account during installation qualification:

- Sets of technical documentation
- Equipment list / maintenance (list of all the equipment used)
- Energy and media supply
- CE-Declaration of Conformity / Manufacture'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 / releases
- Test of operator controls
- Test of control software
- List and testing of error messages

In addition to the above points, the following document must be available, checked and released by the time the OQ is completed at the latest:

- Process flow chart, FMEA, production control plans (PQP)
- Qualification documents of the production equipment used (acceptance protocol, checklist for commissioning, maintenance specifications,..)
- Qualification documents of the used equipment / tools (acceptance protocol, maintenance specifications,..)
- Calibration certificates of used equipment / tools like annealing furnaces, firing chambers, ...
- Measurement system analysis (MSA1 / MSA2) on defined characteristics (see technical specification); method 2 ANOVA
- Quality-relevant process parameters must be determined and their tolerances defined.

The documents mentioned, including the respective results, must be handed over to Ypsomed as part of the process validation, specification in the validation plan per product; or inspection as part of an audit.

With the completion of the OQ, an initial sample test report (EMPB) as well as the MSA1 and MSA2 incl. the associated sample components must be sent to Ypsomed. This EMPB and the samples are assessed by the Ypsomed product development team as part of the design verification process and any necessary STI calculations are performed. Only after Ypsomed has approved the results may the PQ be started.

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 analyses of PQ

The production of the PQ batch(es) should reflect possible events / occurrences of an average production. These include: Material- batch changes, production interruptions, shift changes,.... Production interruptions should be timed to cover different efforts / steps required to restart the equipment (e.g. cooling down a temperature-controlled equipment to room temperature, reheating and restarting the process, removing and cleaning an injection mold).

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

Written approval for series delivery is given by the respective Quality Control employee, following Ypsomed's internal review and approval of the overall documentation.

7 Audit rights

Suppliers that are to be classified as critical / important according to Regulation EU 2017/745 (MDR) (these are primarily suppliers that provide Ypsomed with customer-specific materials that flow into end products placed on the market by Ypsomed) shall ensure that Ypsomed as well as commissioned notified bodies and the authorities responsible for Ypsomed's end product are granted access to the operating sites related to Ypsomed products.

These may also be unannounced audits by notified bodies / authorities without prior notice; see Regulation EU 2017/745 (MDR). The supplier shall ensure that unannounced audits are carried out by notified bodies / authorities and shall grant them access to the production facilities and to all documentation relating to Ypsomed products at all times.

Details on the right to audit can be found in Appendix 7.

8 Annex

The above documents can be provided upon request. Please get in touch with your known contact at Ypsomed.

Annex 1 Template 8D Report

Annex 2 System qualification and process validation

Annex 3 Validation Plan

Annex 4 Initial Sample Inspection Report

Annex 5 Qualification

Annex 6 Measurement System Analysis MSA

Annex 7 Information sheet for suppliers - unannounced audits