

Question & Answers

Preamble

Q: Is this guide mandatory /legally binding?

A: This guide is not mandatory neither legally binding, but it will support the user in evaluating the quality systems at the RSM supplier. If some of the requirements are not in place, a risk-based evaluation should be done to define the impact on the involved product.

Q: Do we need to audit RSM suppliers?

A: Auditing is not a legal requirement. However, it is important to evaluate the Quality System of the RSM supplier as part of the supplier qualification. There are different options to perform this (audit, questionnaire, ...).

The following criteria can be used (not limited):

- complexity of the molecule
- number of manufacturing steps between RSM and API
- knowledge of the supplier (e.g. past experience)
- worldwide available or custom made
- continuous process or single campaigns
- dedicated or multipurpose equipment

The decision not to audit can be overruled at a later stage in function of specific events such important quality related issues, regulatory actions against the supplier.

Q: Do audits have to be performed exclusively by members of the quality unit?

A: Quality Auditing is the exclusive authority of members of the Quality Unit. In certain cases, other departments (e.g. Purchasing, Technical operations, R&D) can visit suppliers in support of supplier selection. These visits, when not attended by Quality unit persons cannot replace audits. Moreover, the final approval of a supplier is the responsibility of the Quality Unit.

Q: What if a supplier refuses an on-site audit, while the audit is mandatory according to your procedures and/or risk-assessment?

A: In case a supplier refuses it is very important to understand the reason for the refusal. A refusal can be due to several reasons

- Confidentiality, e.g. in case the audited company is a competitor
- Business related, e.g. volume purchased is too low
- Suppliers concerned they may not fulfil the expectations of the auditors

If, despite further discussion/ negotiation or alternative solutions (e.g. audit by third party) the refusal still remains, a documented risk evaluation should be performed in order to decide on further actions (additional questionnaires, additional testing/sampling upon receipt of the material, on-line interview/audit or change supplier).

Q: Do we need to audit distributors instead of suppliers?

A: You need to evaluate (audit or alternative) the manufacturing site. In addition, if the distributor has specific quality responsibilities that can impact the product (specific storage or transport conditions, dispensing/repacking/re-labelling of the product, testing of the product), they also need to be evaluated (audit or alternative depending on the risk assessment).

Q: What if the suppliers don't want to provide information on the manufacturing process?

A: A high-level ROS description of the RSM is needed from a regulatory perspective to complete your registration file and to evaluate the impact towards the quality of your API. If no information or too limited information is provided, another RSM supplier with a known ROS should be selected.

Chapter 3:

<3.1>

Q: What if there is no quality unit at the RSM supplier?

A: In the scope of this guide a person (or group of persons) that can take independent decisions related to quality can be considered as a quality unit.

Clear roles and responsibilities of this person (or group of persons) should be documented.

Chapter 4:

<4.1>

Q: Should training of contractors be documented?

A: Yes, the level of the training and its documentation depends on the criticality of the activities performed and it should not be based on the individual (permanent worker or contractor) who performs the activities.

Chapter 5:

<5.3>

Q: Are manufacturing operations in 'open' or 'partly-open' environment allowed?

A: Yes, it can be acceptable under the condition that there is a control strategy in place, e.g. mobile protection devices, (dis)charging devices, filtration or distillation in downstream processes, ...

Chapter 6:

<6.3>

Q: Is a calibration certificated by the government (without raw data) enough to consider equipment as calibrated?

A: Yes, if the local governmental practices doesn't allow to provide the raw data of the calibrations. However, the calibration certificates should always be internally reviewed and approved.

Chapter 8:

<8.21>

Q: Does the RSM supplier has to test all incoming raw materials?

A: A process should be in place to evaluate if testing is appropriate or not.

For those raw materials evaluated not appropriate to be tested, other controls can be in place. Examples are:

- Review of certificate of conformity (e.g. for basic chemicals obtained from continuous manufacturing)
- Review of CoA from the supplier against the internal specifications
- Downstream testing (e.g. IPC testing, intermediates testing).
- ...

Chapter 12:

<12.4>

Q: Do you need to perform ICH stability tests to define expiry or re-test dates?

A: No. Data to define expiry or re-test dates can also be based on literature, historical data, retest of retention samples/stocks, ...

<12.13>

Q: Does the RSM supplier need to validate the analytical methods for testing the RSM?

A: Not necessarily. It is the user of the RSM that is responsible that the RSM is released based on test data obtained by validated test methods. Only in case the user is not generating own test data but relies on supplier COA data (i.e. reduced testing) it is necessary that these data are obtained by validated methods and that the supplier is qualified to run them.

Chapter 11

<11.2>

Q: Can a RSM be distributed under quarantine?

A: When evaluating (or auditing) a supplier it should be checked that RSM supplier's procedures do not allow distribution under quarantine without customer's approval.

As an exception and under specific conditions, a RSM can be distributed under quarantine

- if agreed in a documented manner by both parties (RSM supplier and the receiver)
- and if the product is released by the RSM supplier before your internal use.