ICH Q8 / Q9 / Q10

with GMP and ISO-9001 references

INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED TRIPARTITE GUIDELINES:

Q8 (R2) PHARMACEUTICAL DEVELOPMENT (Aug 2009)
Q9 QUALITY RISK MANAGEMENT (Nov 2005)
Q10 PHARMACEUTICAL QUALITY SYSTEM (Jun 2008)

with paragraph references to:
- 21 CFR 210 / 211
- EU GMP Guide Part I
- ISO 9001

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How to use this document

We have compiled the three Q-guidances from ICH together with a reference matrix as a tool to get an overview of four basic enablers and Quality System elements.

We have choosen these four elements since they represent areas that may not be a part of a traditional GMP-based model. Since implementation of the concepts described in Q8/Q9/Q10 may result in potential opportunities as described in Annex 1 to the Q10 Gudiance, we believe this can be a useful tool.

Management controls

Quality by Design

Quality Risk Management

CAPA-system

Each of these four element has it's own color code marking (see above)

You can find where that particular element is discussed in the three ICH-documents by looking for the color markings in the text.

In the Matrix in the beginning you can also see references to those four elements as they are described in the EU Guide to GMP, in 21 CFR 210/211 and in ISO 9001:2008.

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Management controls, ICH references			Other GMP references		
ICH Q8(R2)	**ICH Q9**	**ICH Q10**	**210/211**	**EU Part I**	**ISO9001**
NA	4.1	1.3	210.1(b)	1.1-1.3	1.1-1.2
	4.4	1.7	211.22	2.1-2.7	4.1-4.2
	4.5	1.8	211.25	4.24	5.1-5.6
	4.6	2.1 - 2.8	211.180(e)		
	II.1	3.2	211.180(f)		
	Glossary	3.2.4 & Table IV			
		4.1			
		4.2			
		4.3			
		Glossary			
		Annex II			

equipment, input materials) with potential to have an impact on product quality, based on prior knowledge and initial experimental data. For an illustrative example, see Appendix 2. The initial list of potential parameters can be quite extensive, but can be modified and prioritized by further studies (e.g., through a combination of design of experiments, mechanistic models). The list can be refined further through experimentation to determine the significance of individual variables and potential interactions. Once the significant parameters are identified, they can be further studied (e.g., through a combination of design of experiments, mathematical models, or studies that lead to mechanistic understanding) to achieve a higher level of process understanding.

2.4 Design Space

The relationship between the process inputs (material attributes and process parameters) and the critical quality attributes can be described in the design space (see examples in Appendix 2).

2.4.1 Selection of Variables

The risk assessment and process development experiments described in Section 2.3 can lead to an understanding of the linkage and effect of process parameters and material attributes on product CQAs, and also help identify the variables and their ranges within which consistent quality can be achieved. These process parameters and material attributes can thus be selected for inclusion in the design space.

A description should be provided in the application of the process parameters and material attributes considered for the design space, those that were excluded, and their effect on product quality. The rationale for inclusion in the design space should be presented. In some cases it is helpful to provide also the rationale as to why some parameters were excluded. Knowledge gained from studies should be described in the submission. Process parameters and material attributes that were not varied through development should be highlighted.

2.4.2 Describing a Design Space in a Submission

A design space can be described in terms of ranges of material attributes and process parameters, or through more complex mathematical relationships. It is possible to describe a design space as a time dependent function (e.g., temperature and pressure cycle of a lyophilisation cycle), or as a combination of variables such as components of a multivariate model. Scaling factors can also be included if the design space is intended to span multiple operational scales. Analysis of historical data can contribute to the establishment of a design space. Regardless of how a design space is developed, it is expected that operation within the design space will result in a product meeting the defined quality.

Examples of different potential approaches to presentation of a design space are presented in Appendix 2.