Dear Madam,
dear Sir,

we Regiomedica GmbH, herewith take the opportunity to provide you with comments regarding the "Review of the Variation Guideline".

Comment 1

B.II.b.3 Change in the manufacturing process of the finished product, including an intermediate used in the manufacture of the finished product.

Comment:
While the term "intermediate" is well defined in the area of drug substance manufacture (*see below) it is considered to be not clearly defined for the manufacture of drug products.
It is therefore suggested to provide a definition of "intermediate" to be used in the context of the above change fact.

*CPMP/QWP/130/96, Rev. 1
Intermediates:
Information on the quality and control of intermediates isolated during the proces should be provided. For key intermediates which are those which influence final quality of the active substance the analytical methods used to control them should
be suitably validated if they are non-compendial.

Comment 2

B.II.d.1 Change in the specification parameters and/or limits of the finished product

Condition 1: The change is not a consequence of any commitment from previous assessments to review specification limits (e.g. made during the procedure for the marketing authorisation application or a type II variation procedure), unless the supporting documentation has been already assessed and approved within another procedure.

Comment:
The wording of this condition as it is currently written is confusing. Does the condition mean that if the change is the result of a commitment where the supporting documentation has been already assessed and approved within another procedure, then this condition is not fulfilled? Please rewrite this condition to make it clear and unambiguous.

Thank you very much for considering these comments and providing clarification.

Kind regards,

Matthias Finkler

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