

therefore should be monitored or controlled to ensure the process produces the desired quality (ICH Q8R1).

**Critical Quality Attribute (CQA):**

A physical, chemical, biological or microbiological property or characteristic that should be within an appropriate limit, range, or distribution to ensure the desired product quality. (ICH Q8R1)

**Continuous Quality Verification (CQV):**

An approach to process validation where manufacturing process (or supporting utility system) performance is continuously monitored, evaluated and adjusted as necessary. It is a science-based approach to verify that a process is capable and will consistently produce product meeting its pre-determined critical quality attributes. (ASTM E2537)

**Design space:**

The multidimensional combinations and interaction of input variables (e.g. material attributes) and process parameters that have been demonstrated to provide assurance of quality. Working within the design space is not considered as a change. Movement out of the design space is considered to be a change and would normally initiate a regulatory post-approval change process. Design space is proposed by the applicant and is subject to regulatory assessment and approval. (ICH Q8 and ICH Q8R1) [NOTE: Q10 definition is limited to the first sentence above]

**PAT**

A system for designing, analyzing and controlling manufacturing through timely measurements(i.e during processing) of critical quality and performance attributes of raw materials and in-process materials and processes with the goal of ensuring final product quality (ICH Q8 R1/FDA definition)

**Quality by Design (QBD):**

A systematic approach to development that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management. (ICH Q8 R1).

**General Guidance**

Real Time Release encompasses more than just end product test replacement. It considers building a level of understanding of the manufacturing process that allows definition of the important parameters and attributes that need to be monitored and controlled to ensure quality. Real time release is a product of this requisite process understanding and an effective process control strategy.

The following graphic shows the key elements of any RTR strategy:

**Figure 1: [Key Elements of a RTR Strategy](#)**

In any RTR testing strategy it will be key to demonstrate process understanding and to develop a process monitoring and control plan to assure the quality of critical quality attributes based on this process understanding and on knowledge of the process boundaries.

Additional guidance on each step can be found in section 4.0 of this guidance.