Driving Change in Quality

Process Validation Principles

Principles

Principles

A “process” is a series of actions or steps taken in order to achieve a particular end. Like a bottle filling process...

Principles

Closure

Level

Label

“Validation” is the action of checking or proving the validity or accuracy of something... in the case of bottle filling, is the checking that all bottles contains the required qualities like: level, label, and closure, among others...

Principles

Process Validation

Documented Actions

Process validation is the set of documented actions used to prove that the qualities of the product, resulting from a process, are as consistent as they are required to be.

Principles

Through process validation, we provide assurance of product quality. Since sometimes each and every product cannot be tested, process validation uses statistical certainty to show that all products manufactured meet requirements.

Principles

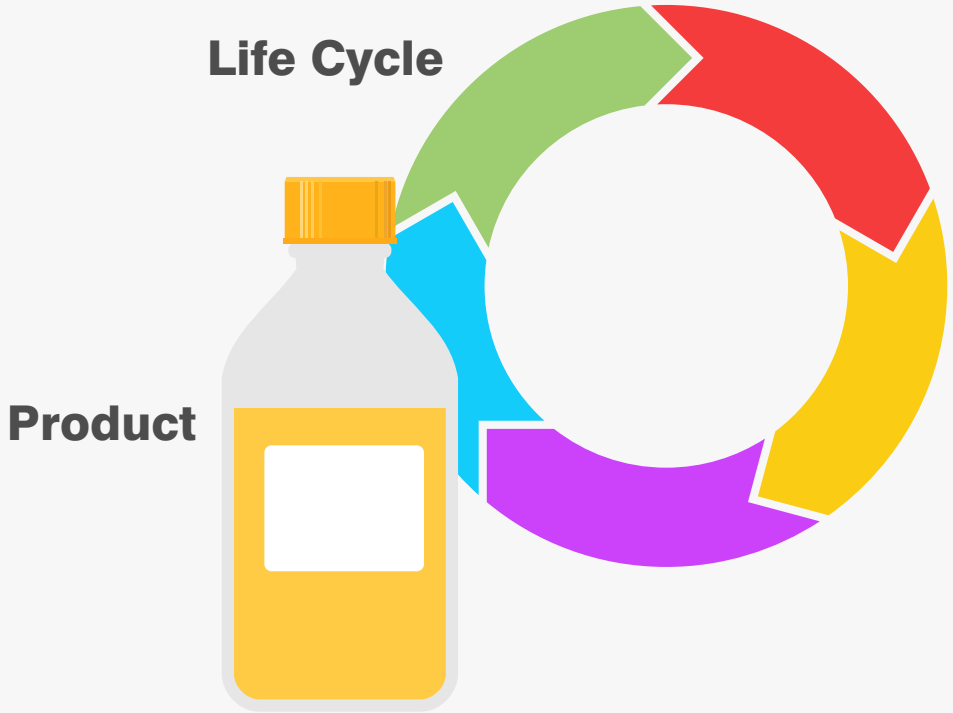
Regulatory Agencies

Clients

Certification Institutions

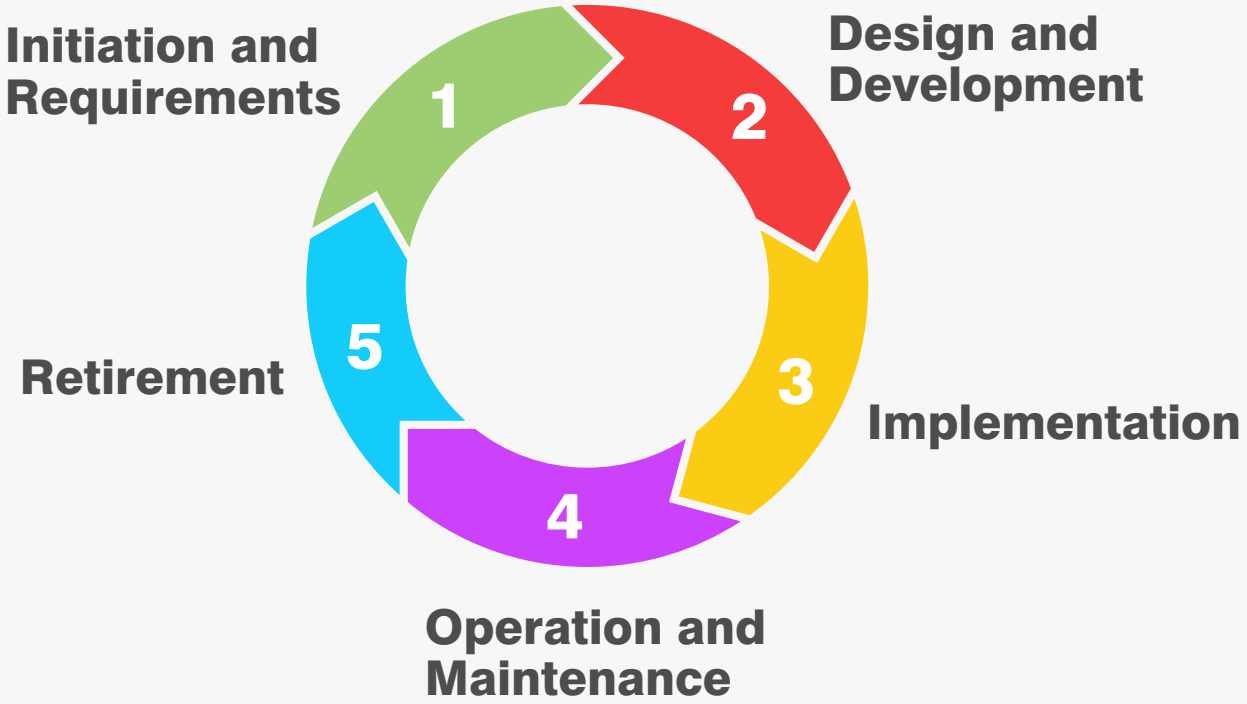
Validation answers to the expectations of clients of having a quality product... and to the requirements of regulatory and certification agencies.

Principles



To understand process validation it is necessary to understand the concept of product life cycle. In the context of a product, life cycle is the series of stages through which the product passes during its lifetime, from initiation to retirement.

Principles



In the context of a product, life cycle is the series of stages through which the product passes during its lifetime. These are: Initiation and requirements, design and development, implementation, operation and maintenance, and retirement.

Initiation and Requirements

Initiation and Requirements

The initiation and requirements stage starts when a need or opportunity is identified, for example by a market researcher with the clients in the field. An example of a product need or opportunity can be a new reagent for genetic analysis.

Initiation and Requirements

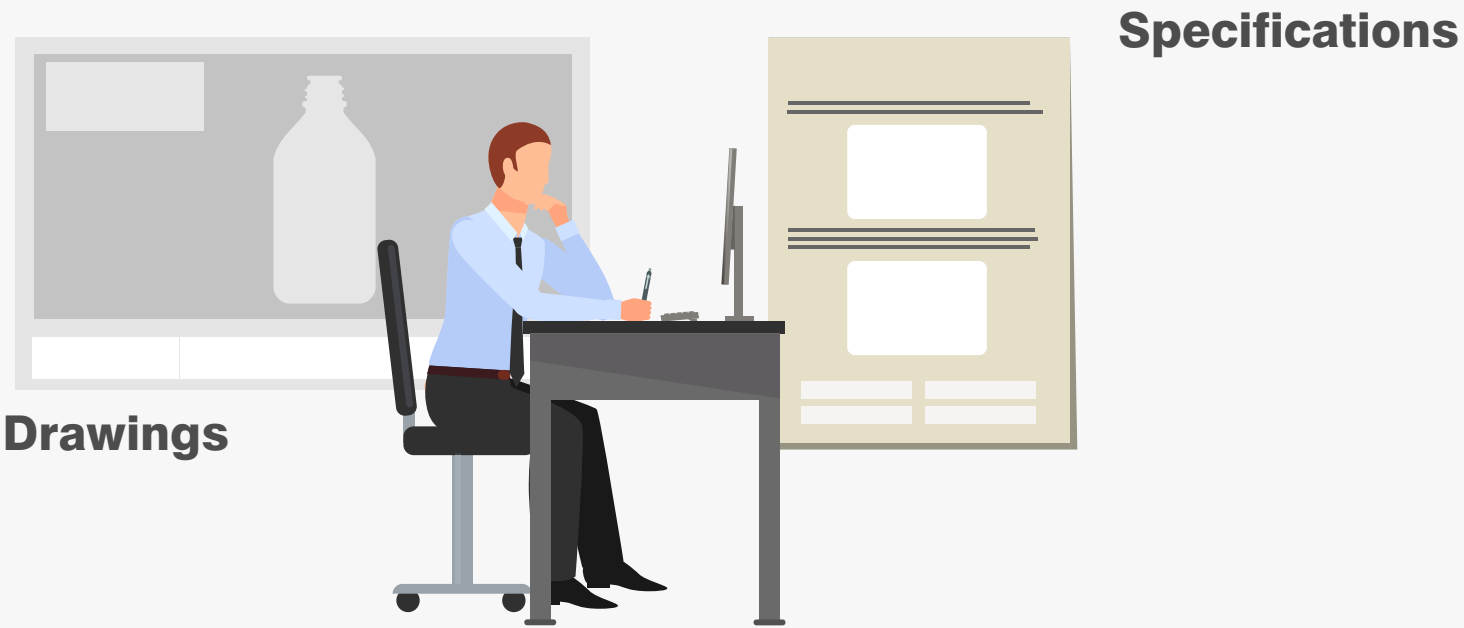
Concept

Requirements

The product opportunity becomes a concept when a description of the product with a set of requirements is developed. Examples of requirements are the reagent functionality, performance, appearance, and stability.

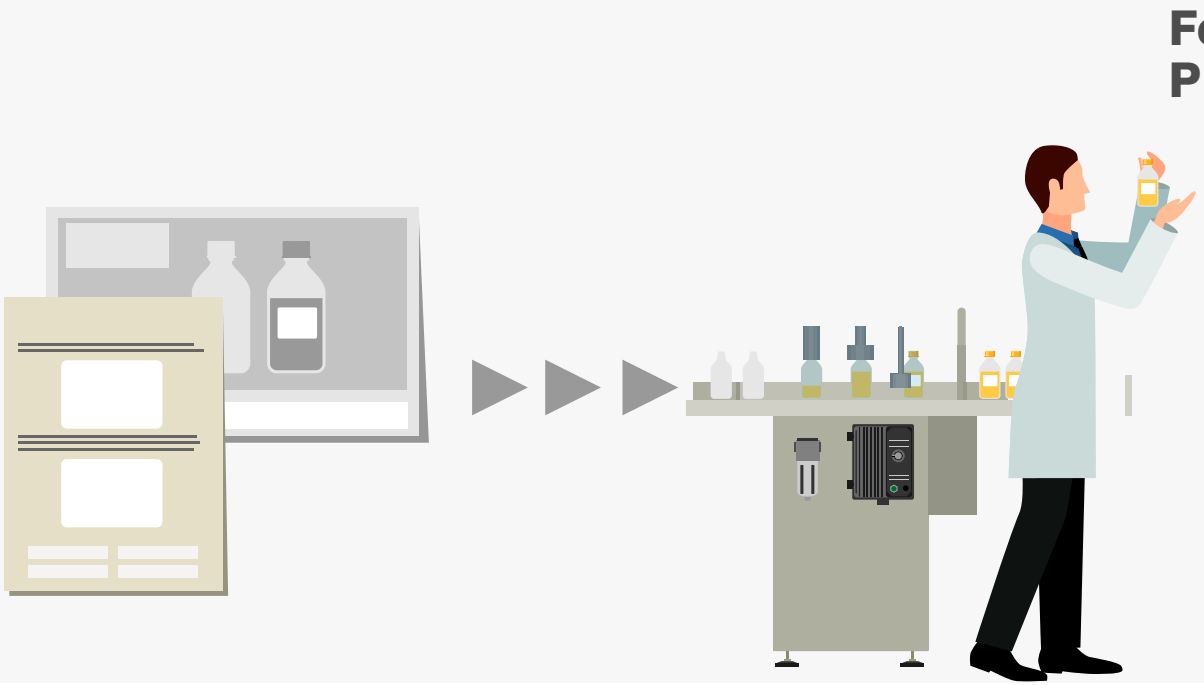
Design and Development

Design and Development



During the design, the concept and requirements are transformed into drawings and specifications that describe how the product will deliver the required functionality.

Design and Development



During development, the design is converted into a feasible product. The development phase further defines the product with additional specifications based on scientific work.

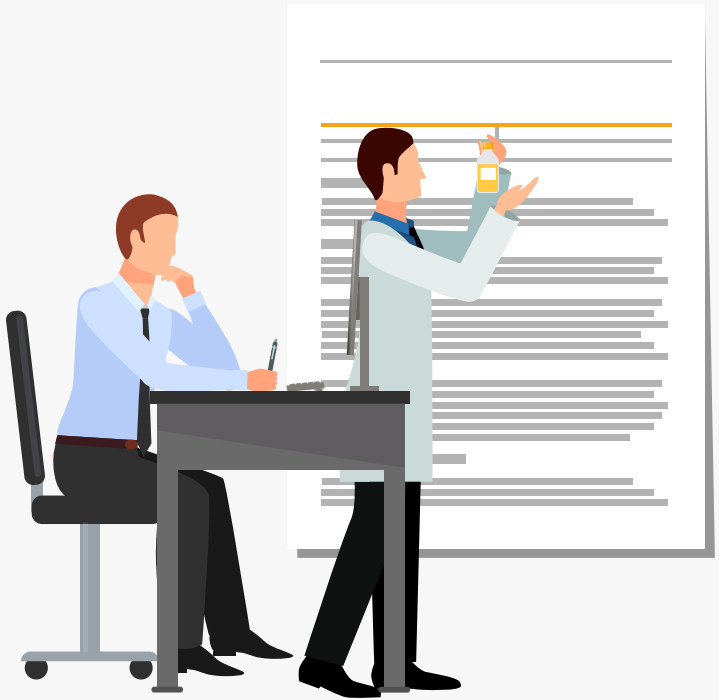
Design and Development

Pilot Size System

Statistical Analysis

The feasibility studies are based on statistical analysis of the production data at this stage. This is mostly done in pilot-size systems, the statistical results are used for the translation of the pilot process into production-size systems.

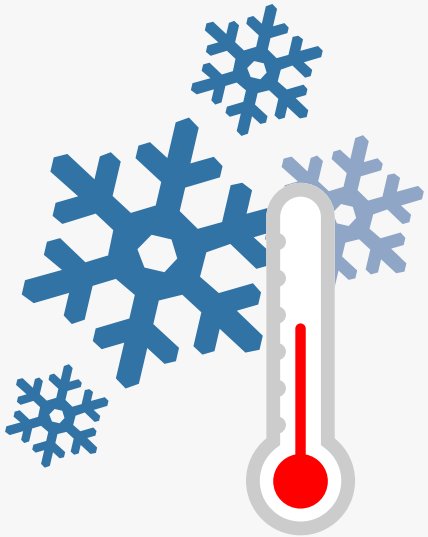
Design and Development



Design and Development Procedures

Each step of design and development needs to be controlled through design and development procedures to ensure the product meets all design characteristics and attributes.

Design and Development

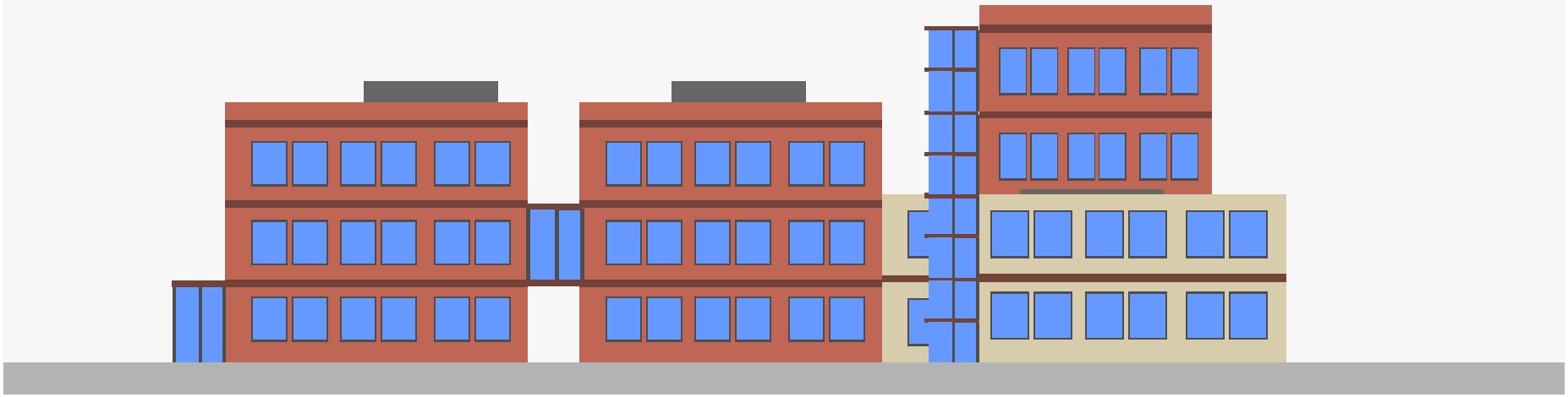


Environmental Conditions

Environmental conditions for production, such as filling and storage temperature, are defined in the development phase...

Design and Development

Facilities and Utilities



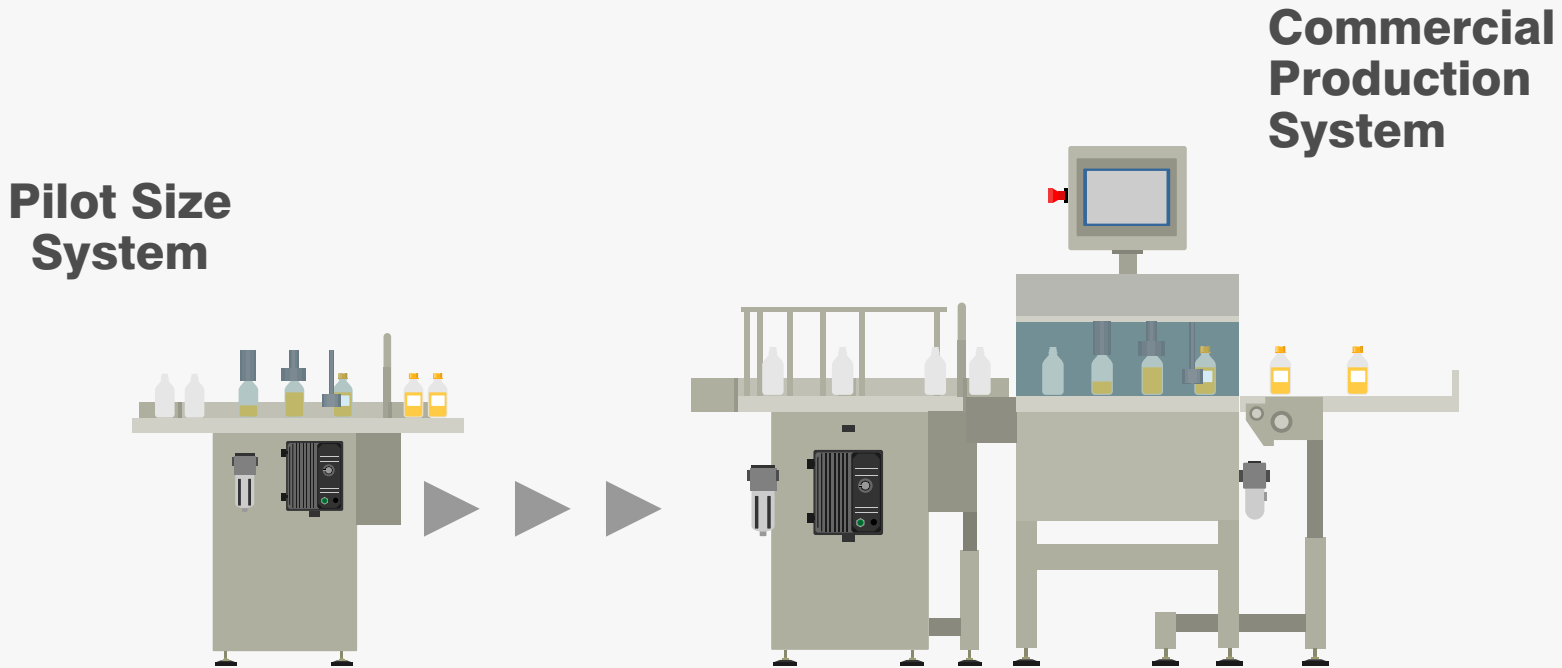
... as well as the facilities, environment, and utilities necessary to support to the production operations...

Design and Development

The development phase creates data sheets with development information that is later refined into final specifications and the initial version of the operational procedures.

Implementation

Implementation



In the implementation stage, the laboratory or pilot-scale models are translated the commercial production systems.

Implementation

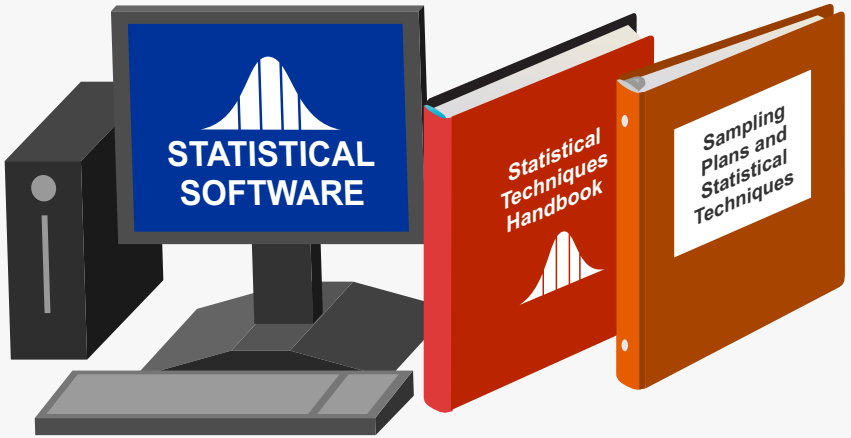
Process Validation

Commercial Production System

Is in the production environment where the final verification is carried out. This final verification is what is commonly known as process validation...

Implementation

Statistical Tools



For process validation, it is necessary to obtain expertise applying statistical tools for the sampling analysis of the manufacturing data.

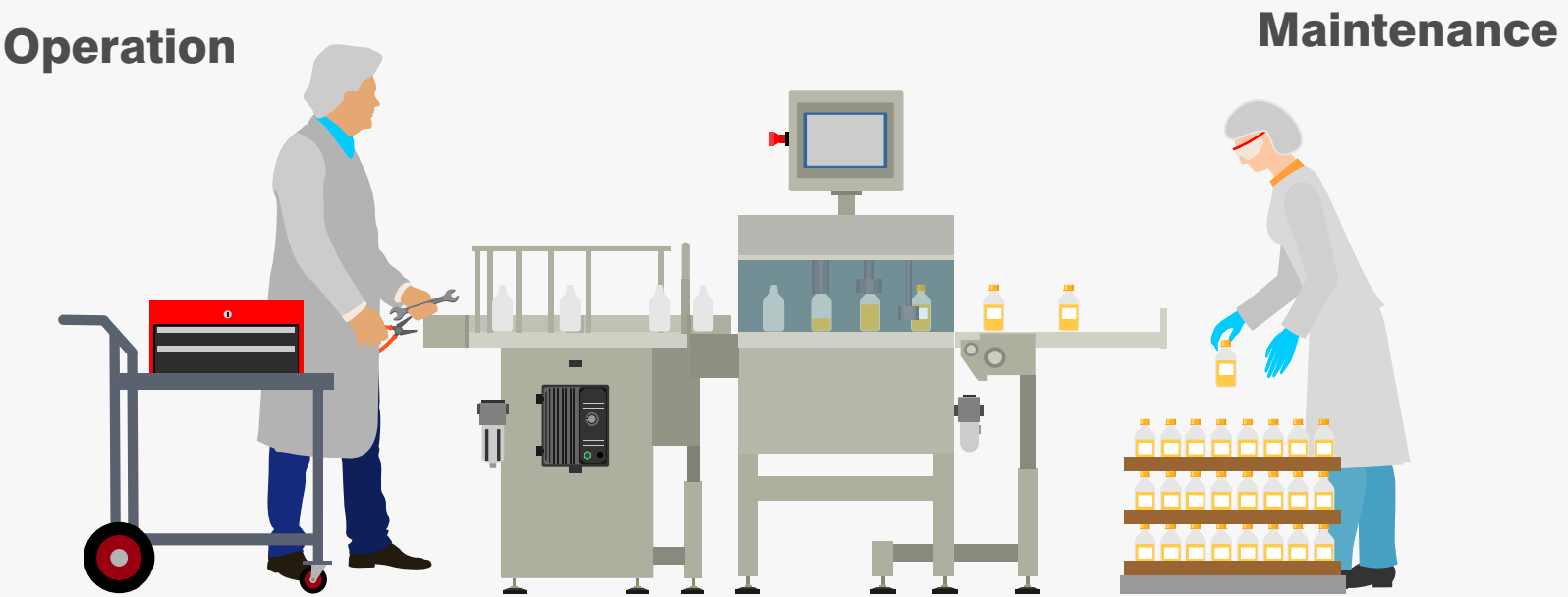
Implementation

Consistent Quality

Assurance

... that way, at the end of the implementation stage, the company should have sufficient understanding and data to provide a high degree of assurance of the consistency of the manufacturing process in the long term.

Implementation



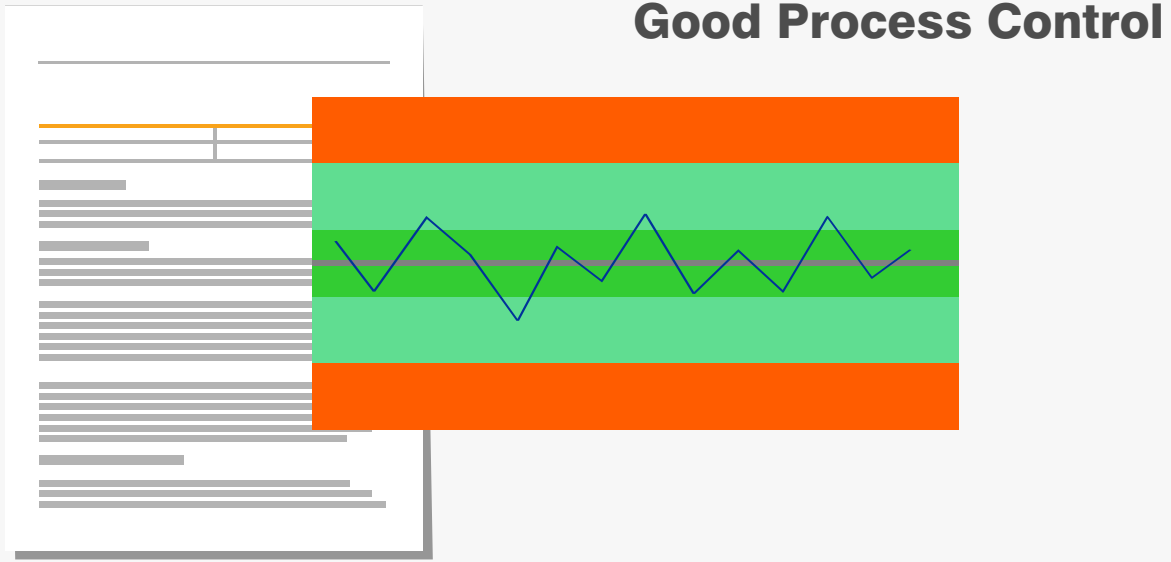
The operation and maintenance activities need to be contemplated during process validation.

Implementation

Final Operation and Maintenance Procedures

While the initial operational and maintenance procedures are used for the validation, the experience of the validation exercise is then used for the development of the final operational and maintenance procedures.

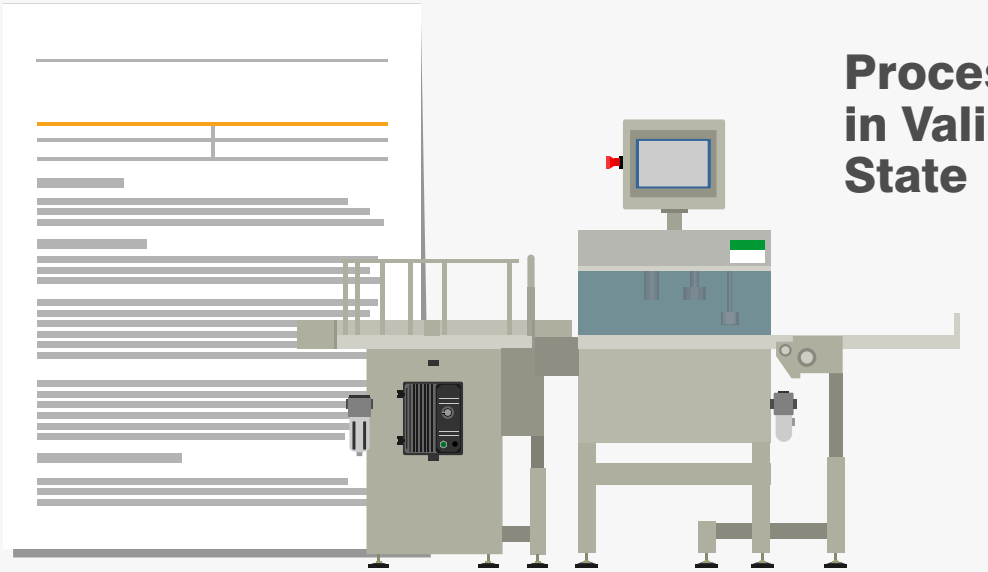
Implementation



Good operational procedures are the basis of good process control.

Implementation

Maintenance Procedures

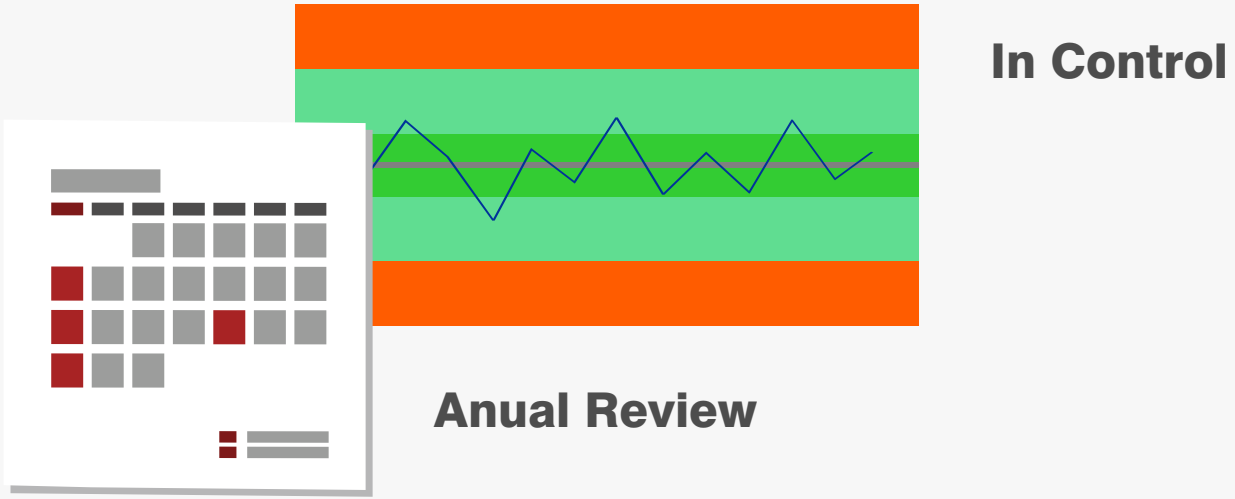


Process in Validated State

Clear maintenance procedures are necessary to assure that maintenance activities do not affect the validated state of the process.

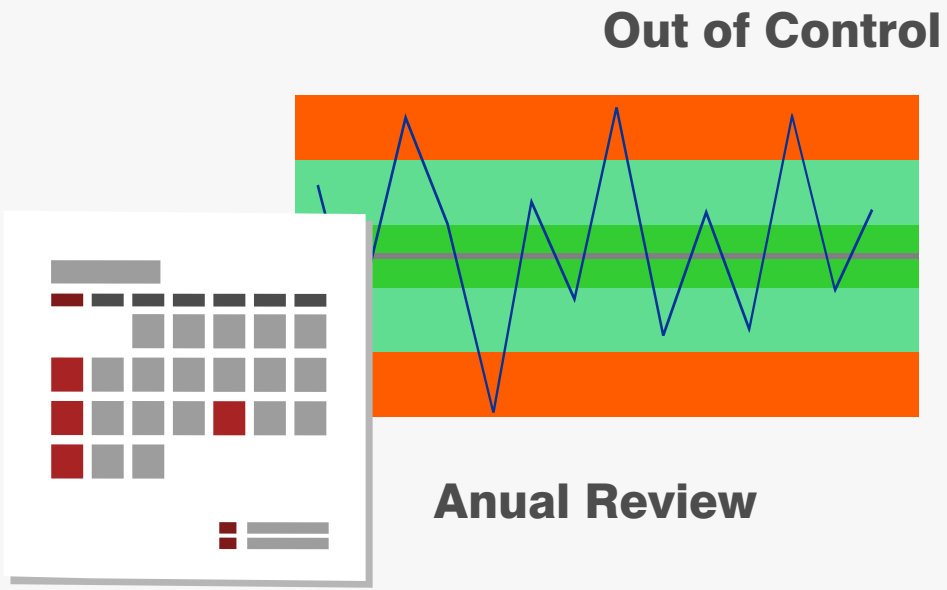
Operation and Maintenance

Operation and Maintenance



To maintain the validation state, the annual review data for a validated process should show that the process remains in a state of control.

Operation and Maintenance



Periodically evaluating the performance of the process identifies problems and determines whether action must be taken to correct, anticipate, and prevent problems so that the process remains in control. In case the process is out of control, revalidation may be necessary.

Stages of Process Validation

Process Design

Process Qualification

Continuous Process Verification

In summary, process validation is generally conducted in three stages that include: process design, process qualification and continuous process verification.

Retirement

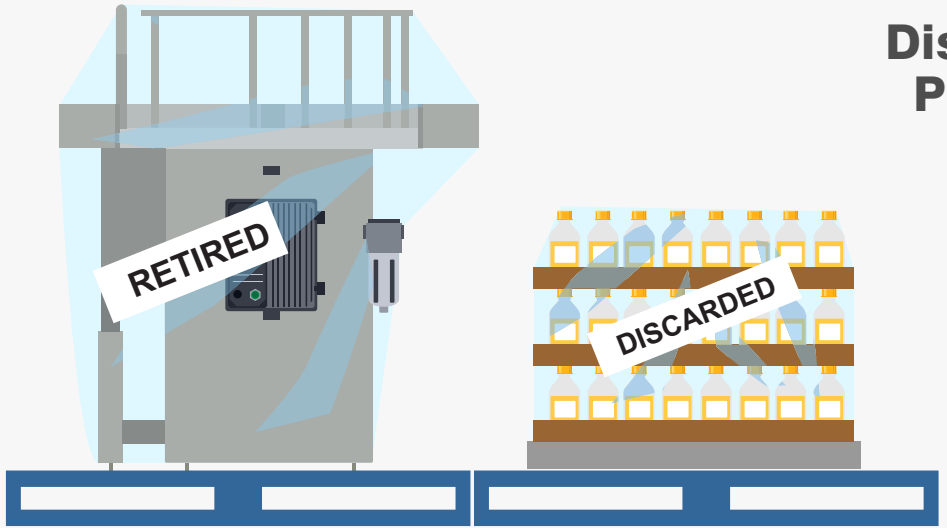
Retirement

Retired Equipment

In the retirement stage, the process is terminated and the process equipment is retired or re-purposed...

Retirement

Retired Equipment



Discarded Product

...all remaining material is accounted for and its condition monitored until it is completely disposed of by use or adequate destruction.

Retirement

Closed Validation

Process validation monitoring needs to be continued until the retirement phase. At that stage the validation process is closed.

Quality by Design

Quality by Design

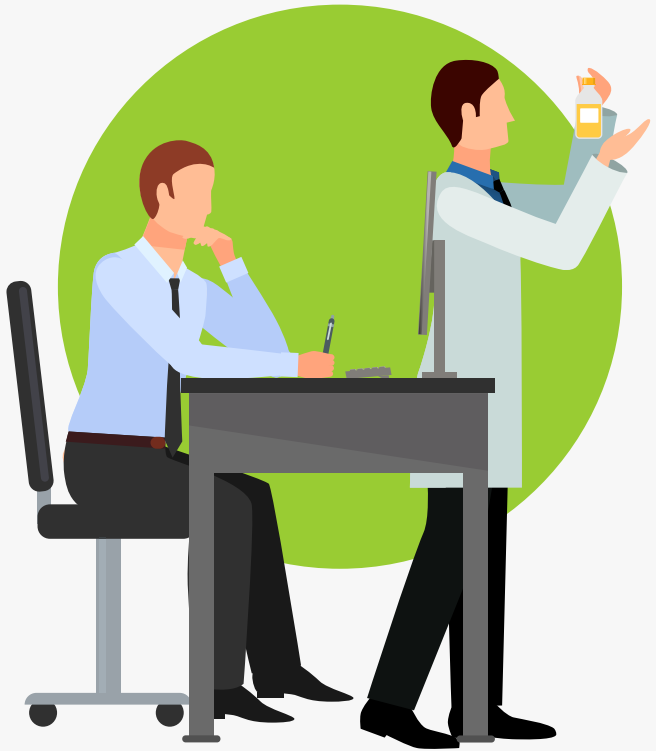
Quality
by Design

Level
of
Emphasis

Quality
by Testing

Modern process validation requires that the emphasis is placed in the design and development and not on the operations and maintenance. This approach is known as Quality By Design as opposed to Quality by Testing.

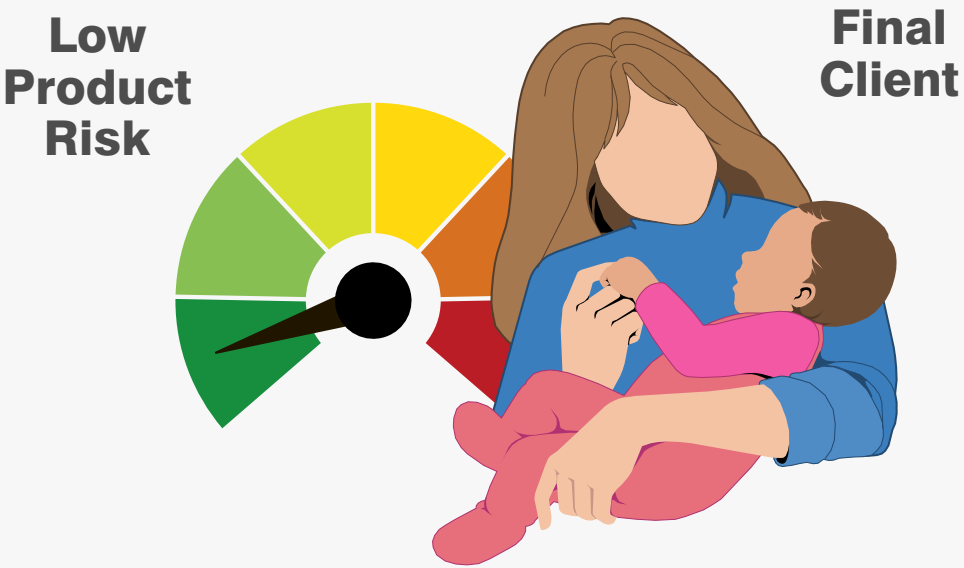
Quality by Design



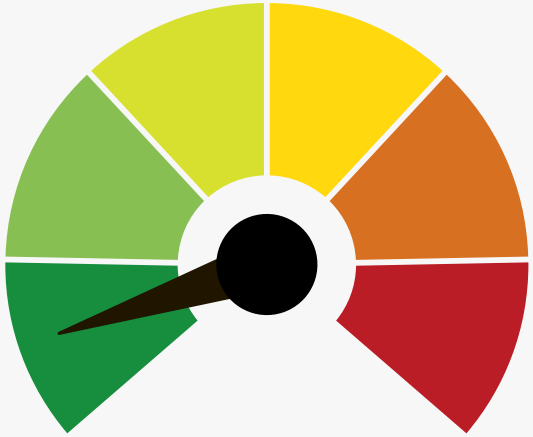
Quality by Design

In this way, quality is assured in the beginning of the product life cycle.

Quality by Design



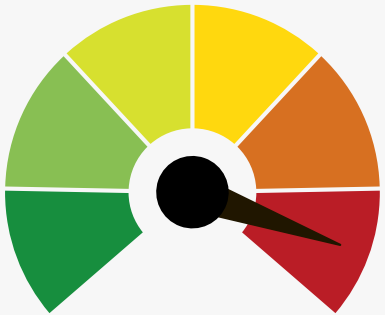
Quality by design is a risk-based approach that uses solid scientific and engineering principles with the purpose of creating a product with a minimum of risk for the client.



Risk-Based Approach

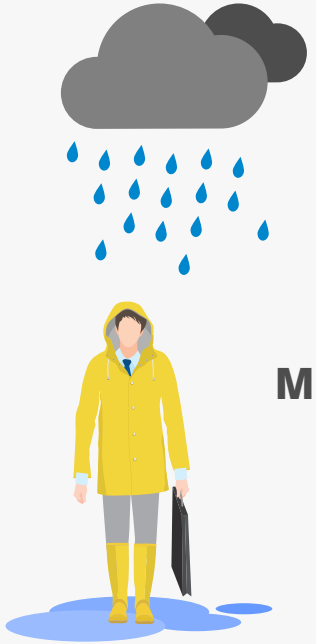
Risk-Based Approach

High Risk



To understand the concept of risk lets see an example using the risk of being hit by lighting. If there are thunderstorms and we go out with and umbrella, there is a high risk of being hit by lighting.

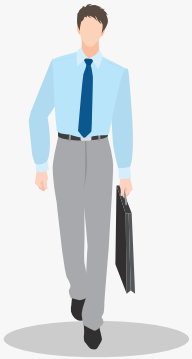
Risk-Based Approach



Mitigated Risk

If it is only raining and we go out with a raincoat the risks are mitigated.

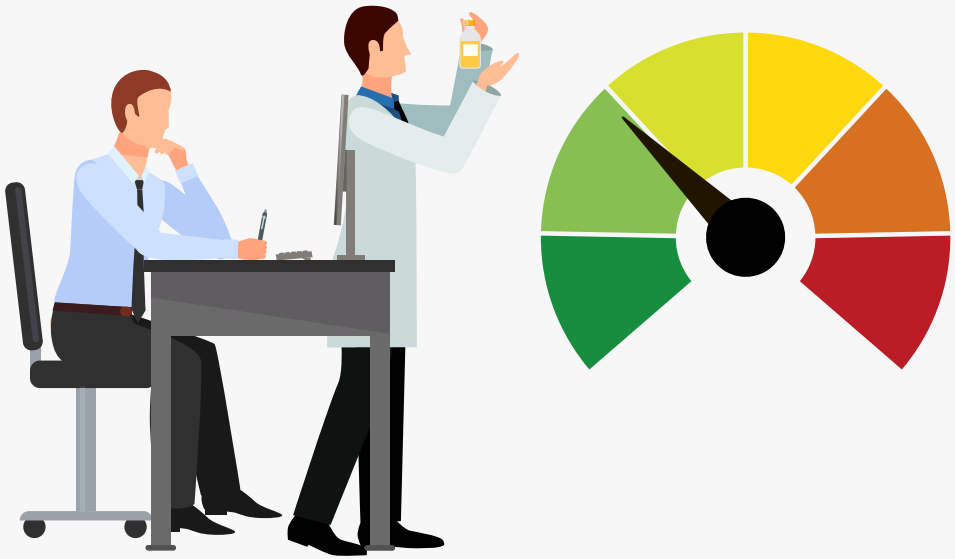
Risk-Based Approach



Mimimum Risk

The minimum risk is represented when we go out only in sunny days.

Risk-Based Approach

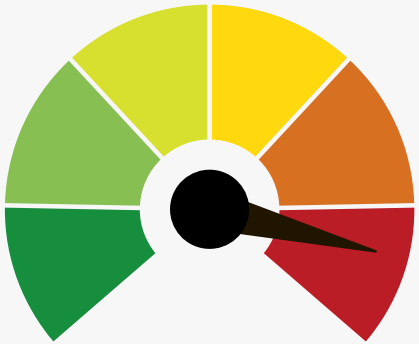


In Quality By Design (QBD) the risks of a process are evaluated in the design and development stages. The level of testing during validation is proportional to the level of risk.

Risk-Based Approach

Maximum Validation Samples

High Risk

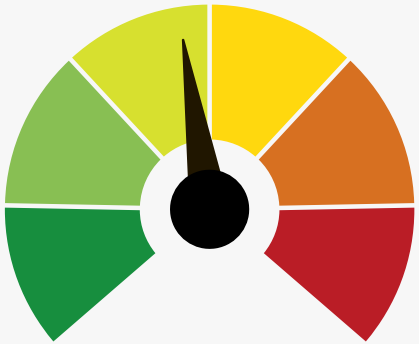


... High risk requires more testing. This is an undesired quality condition since quality cannot be assured merely by in-process or finished-product inspection or testing.

Risk-Based Approach

Less Validation Samples

Mitigated Risk

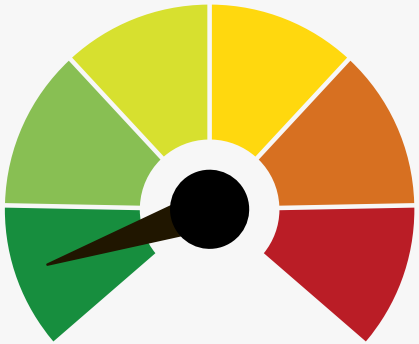


Based on the acceptable risk for the patient, mitigations are defined and implemented, mitigated risks require less testing. Mitigation may come from engineering solutions or from procedures.

Risk-Based Approach

Minimum Validation Samples

Mitigated Risk



In the case of minimum risk to the patient, the testing is also minimal during validation. This is the desired quality assurance condition.

Process Validation Principles

END