

Sterilization Process Monitoring
'In-Pack' Monitoring versus 'Load Control'
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Abstract

This presentation focuses on the rationale and requirements for routine monitoring of sterilization processes. Included in the presentation are discussions on the definition of sterilization and the level of sterility assurance required, parametric release, current and future regulatory requirements, and the benefits of monitoring a sterilization load by means of a 'load control' versus the use of monitoring in each pack or tray within the sterilization load.

Sterilization

Sterilization can only be destructively tested, and therefore it must be based on a probability. In order to achieve this certain key assumptions must first be made.

- The "bioburden", or total microorganism contamination on the load must be known, or estimated – this is usually set at a maximum of 1,000,000 organisms for medical devices.
- *Geobacillus stearothermophilus* is used as the reference organism for steam sterilization processes. This reference organism is assumed to be the most resistant organism to the process.

Sterility Assurance Level

- The degree of "sterility" can be quantified as an SAL, or sterility assurance level.
- SAL is based on the theoretical extrapolation of exponential decay of a reference organism population.

The Sterility Assurance Level, or SAL, is a measure of the confidence in the attainment of sterility:- in other words a probability of 1 unsterile load in 1,000,000.

This is achieved by taking a population of 1000,000 spore inactivating this spore population in good quality steam - this will generally take 1 min at 134°C – this time would then need to be doubled under the same sterilization conditions to achieve a 1 in 1,000,000 chance of an unsterile load as it is unfeasible to try to create a biological indicator with a million spore or to put a million biological indicator 10^6 into the same chamber for the same cycle.

Sterility assurance may be achieved through two different approaches the obvious outcome is the confidence in the attainment of sterility.

These approaches are:
Biological release
Parametric release.

Biological Release

- Includes the use of a biological indicator placed in every load.
- The load is only released after the full incubation of the biological indicator.

Parametric Release

- Requires the pre-validation of all process variables, including loading patterns, load configurations etc.
- Requires verification after process that all parameters and variables were within pre-set defined limits.
- The whole principle of parametric release relies upon the co-ordinated use of physical measurements, chemical and biological indicators.

Therefore to achieve sterility assurance through biological release little or no statistical process control is required, however it is time consuming and expensive as items need to be quarantined while awaiting results of biological indicators. However to achieve sterility assurance through parametric release extensive validation of all variables is required and process parameters need to be constantly monitored - this enables the immediate release of the product.

Physical measurements include the likes of pressure gauges, temperature gauges and pen recorders – in other words apparatus on or in the sterilizer that helps to determine that the correct parameters for effective sterilization were present in the chamber.

Chemical indicators provide:-

- An immediate and accurate result.
- At a low cost compared to a biological indicator.
- As a result are able to detect local conditions at multiple points in the load.

Biological indicators provide:-

- A realistic challenge – the actual physical destruction of a spore population – however it has to be remembered that the destruction of a spore population of 1000,000 spore does not mean that SAL has been achieved as has been previously explained.
- Are only indicative of the conditions in the immediate environment.
- Incubation may take hours or days.

Load Control

This would have initially taken the form of a biological indicator however biological indicators now tend to be used specifically for validation purposes not for routine monitoring. Therefore Process Challenge Devices are currently your most common form of load control.

A load control will provide the assurance that the correct parameters for effective sterilization were present IN the CHAMBER. This physical evidence can be retained and stored with the cycle printout providing proof for your records. Therefore providing an element required for parametric release.

In Pack Monitoring

Generally would take the form of a class D/ 4, 5 or 6 chemical indicator placed in the tray, pack or wrapped item. The classification of the indicator would determine, according to its characteristics, the level of assurance offered. These classifications are defined in EN 867-1 and ISO 11140 –1.

In pack monitoring would provide the assurance, again depending on the classification, that effective sterilization conditions were present WITHIN each TRAY, PACK or WRAPPED ITEM. This physical evidence is seen by the end – user and recorded either in theatre or patients notes. Therefore also providing an element of parametric release.

STANDARDS

Current Practice – EN 554 – Sterilization of Medical Devices – validation and routine control of sterilization by moist heat.

EN 554 – requires a daily steam penetration test and stipulates “Routine testing should be sufficient to give assurance that the parameters are within limits equivalent to those determined during performance qualification”.

Future recommendations

Draft ISO 17665

“Sterilization of health care products – the development, validation and routine control of a sterilization process for medical devices – moist heat”.

This draft ISO standard will ultimately replace EN 554 and will incorporate both ISO 11134 and ISO 13683 thereby leading to a harmonisation of practices around the world including both Europe and the USA and the harmonisation of pharmaceutical/ industrial and health care producers of “sterile product”.

Obviously there is a lot more to ISO 17665 than I could include in this presentation however I have tried to highlight the relevant sections/procedures/recommendations to the presentation.

Draft ISO 17665 – **Product specification** – 17665 requires that the specification for the sterilization of a product shall include:-

- It's product family (i.e. products which present a similar challenge to the sterilization process).
- The packaging of the product.
- The manner in which the product is presented to the sterilization agent, including orientation of the packaged product and loading configuration.
- The limiting value of each process variable that will NOT cause an adverse effect on the performance of the product and it's packaging including:- temperature and time it can maintained.
- Pressure.
- Rate of change of pressure.
- Rate of change of temperature.

The specification for products sterilized by saturated steam shall also include the combination of process parameters, including the period that each is maintained to cause air on surfaces, in cavities and in lumens to be reduced to a level that will not prevent contact with surfaces to be sterilized. A means of demonstrating the presence of moist heat in, or on the product is required.

Draft ISO 17665 Definition of the sterilization process.

The sterilization process is the minimum level of microbicidal effectiveness to be achieved by a sterilization process on and/or within a product shall be specified. This sterilization process shall be established:-

- From data supplied by the manufacturer of the product, and/or the packaging, and/or the sterilizer.
- From similarity with a product that is already assigned to a product family.
- From the development of an operating cycle that will deliver the specified **Sterility Assurance Level**.

ISO 17665 - 8.1.3 – SAL

The SAL attained on and/or within the product during the sterilization process shall:-

- a) Be established by knowledge of the number of bioburden.
 - b) Be defined by demonstrating conformity with the process parameters throughout the holding time selected from an official national or regional pharmacopoeia.
 - c) Be deemed to equal or exceed the requirements in b.
 - d) Be determined by the “overkill” approach.
- It would appear in the case of attainment of SAL through parametric release that option b would be the most obvious method to follow.

ISO 17665 - 12 – Maintaining Process Effectiveness.

Includes

- If the sterilization process employs vacuum, an air leakage test shall be carried out at specified intervals.
- If the sterilization process relies on the removal of air from the chamber in order to achieve RAPID and EVEN penetration of steam into the sterilizer load a STEAM PENETRATION test shall be carried out DAILY.

ISO 17665 – 10 – Routine Monitoring and Control

Routine monitoring and control shall be performed on each operating cycle.

Delivery of the sterilization process to the sterilization load shall be verified by confirming, that within specified tolerances, data obtained during routine processing are the same as data obtained during validation. Recorded data from which a comparison is made includes:-

- Sterilization temperature and chamber pressure during the plateau period.
- Duration of the plateau.
- Sterilization temperature band.
- Chamber temperature and pressure at the beginning and end of each stage of the operating cycle.
- The interpretation of any chemical or biological indicator.

Draft ISO 17665 Summary

It seems that the entire focus of the standard is to obtain effective validation of the sterilization of our loads – in a consistent, reproducible and recordable manner thereby attaining parametric release!!!

So if we return to the original question “Are in-pack monitoring systems and load control monitoring systems complementary or conflicting? - Let us compare the two.

Load Control

- Assurance of the load.
- Physical evidence is inspected and retained within the CSSD before the load is released.
- The chemical indicators used within load control PCDs are classified as class 2/B indicators therefore there is no method of determining the specific characteristics of the different indicators used.

In Pack Monitoring

- Assurance within each pack or tray.
- Physical evidence is inspected by the end user and retained at the point of use.
- Indicators are classified in accordance to their performance characteristics.

From this it should be clear that both systems provide a facet of parametric release and offer added security to the CSSD manager and the end user!!

However

First and foremost you must bear in mind the primary objective:-

To provide as much evidence as possible that the attainment of SAL conditions was achieved in and/or on each and every tray or item processed.

Conclusion

Whatever choices are made there is one vital factor. Just as CSSD managers are required to provide documentary evidence of the effectiveness of processes and procedures undertaken, so the same should apply to those providing assurance and monitoring tools which are then incorporated into that documentary evidence.

There is no doubt that due to budgetary restraints choices have to be made – this presentation was aimed to make those choices a little clearer.