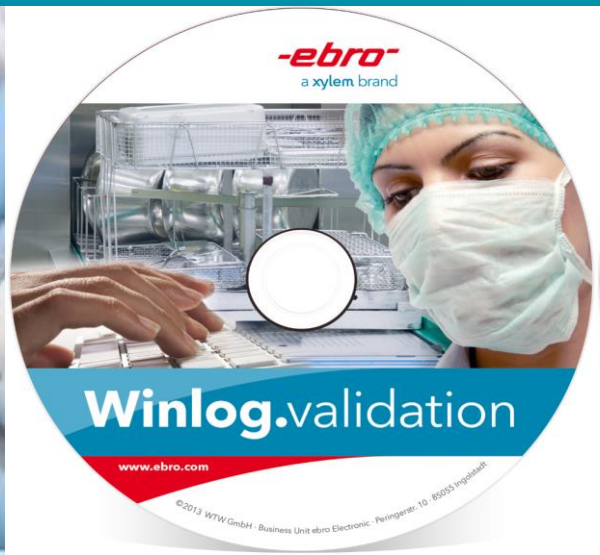
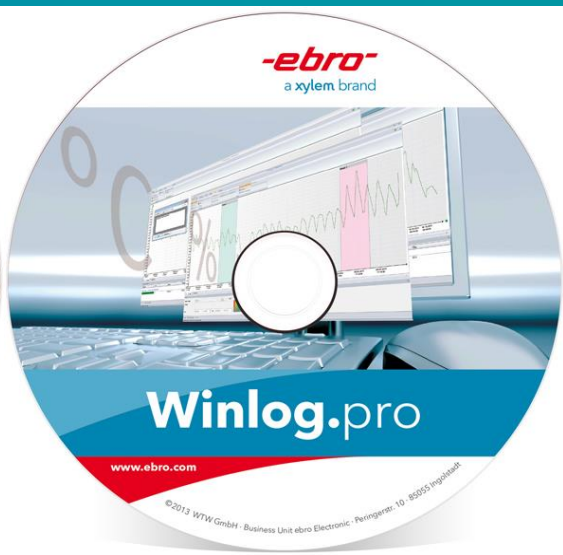
14 February 2020

Ebro Webinar Session P.2:

Practical Solutions for your Routine Monitoring and Validation Requirements





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Webinar Outline:

- Common Sterilization Methods
  - Moist Heat and Dry Heat
  - **EtO Sterilization**
  - H_2O_2 Sterilization
- Process Qualification
- Validation Concepts in Pharma and Healthcare Processes
- Documentation and Compliance

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Your Xylem Analytics Colleagues and Friends wishing everyone and your families all the best and good health amidst the current COVID19 pandemic

"Three things in life – Your Health, Your Mission, and the People You Love and that is it"

- Naval R.

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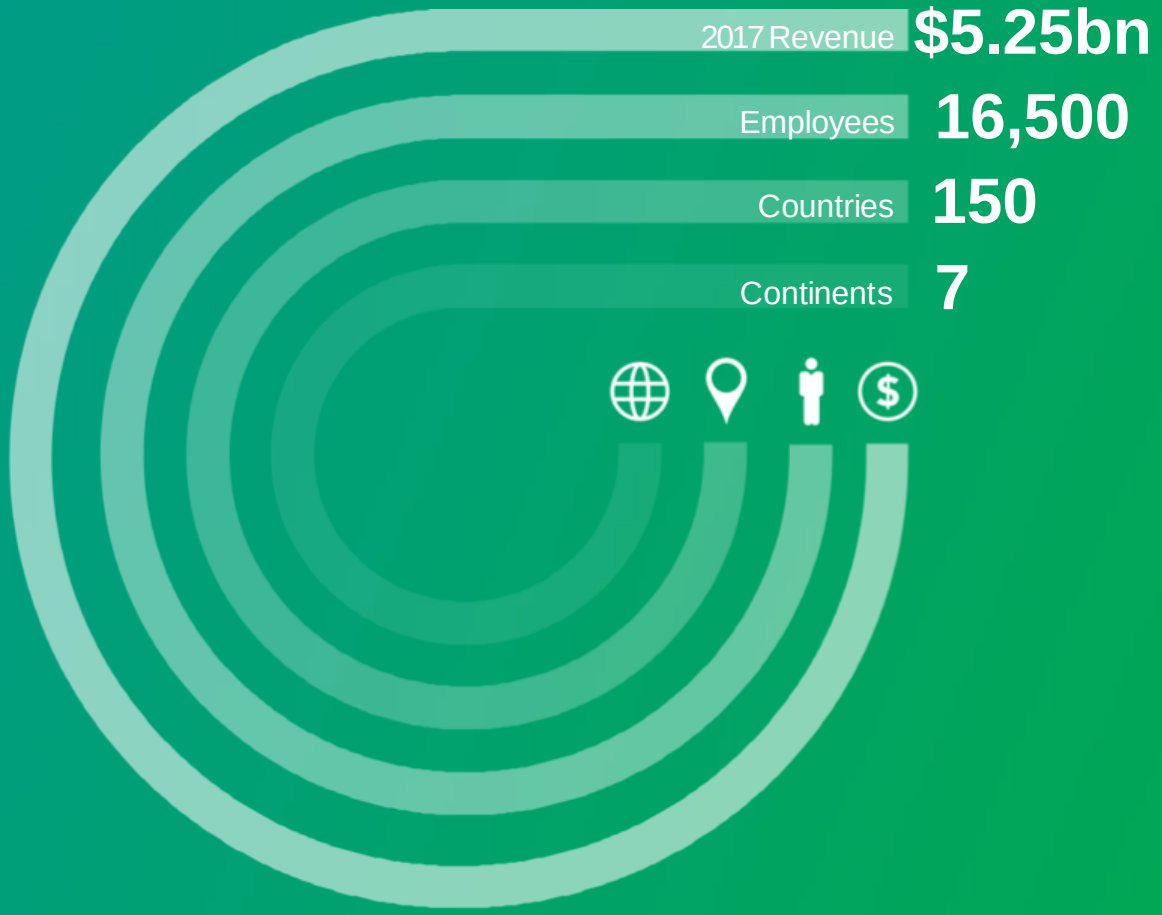
Who is Xylem?

We are one of the world's leading water technology companies



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Bringing together the most progressive brands

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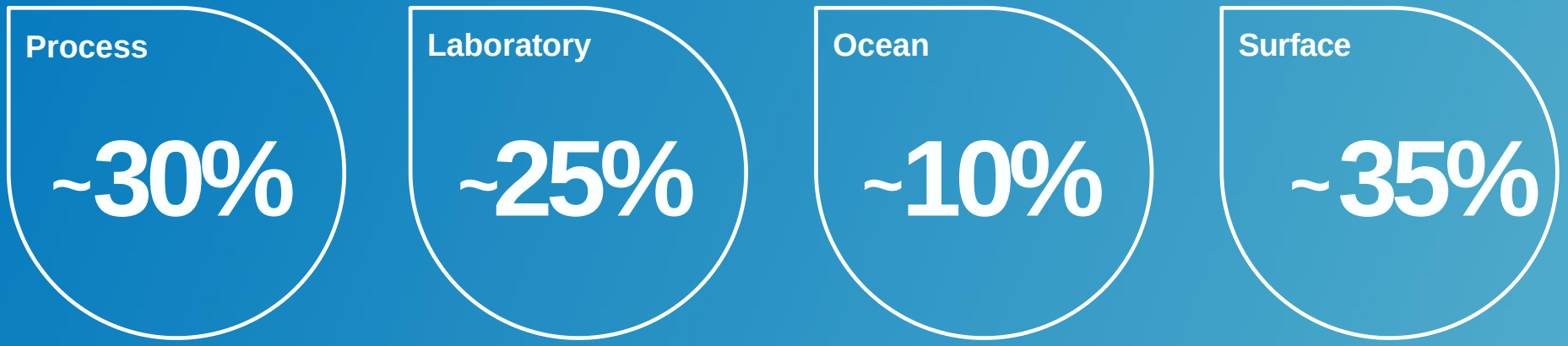
Xylem Analytics Breakdown



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Brush-up on last week's session

BULK SUPPLY

General Store

Clean Receipt

Wards & Units

Dirty Receipt

OPERATING THEATER
PATIENT ROOMS

Disassembly

Washer + Disinfectors

Instruments

Gloves

Rubberwares

Cotton, Gauze, etc.

Assembly

Inspection

Pre-Sterile Storage

Sterilization

Sterile Storage

Distribution

Central Sterile Services Department
Disinfection and Sterilization

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Sterilization Methods & Processes in Pharmaceuticals and Healthcare industries:

- Different cycles & procedures, the same objectives
- Spore Reductions, Microbial inactivation
- Ensure commercial distribution of Sterile goods
- Quality without compromising on Safety

The only objective not common to hospital operations therefore not absolute microbial destruction

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…*Flattening the COVID19 spread What we need?*

- *Sanitation and Disinfection*
- *Use of appropriate PPEs (prevent transmission)*
  - *Coverall, goggles, face shield, gloves head covers and disposable shoe covers*

- *The most common PPE used by people:* Face Masks to filter aerosols

* Aerosol – Suspension of Tiny particles

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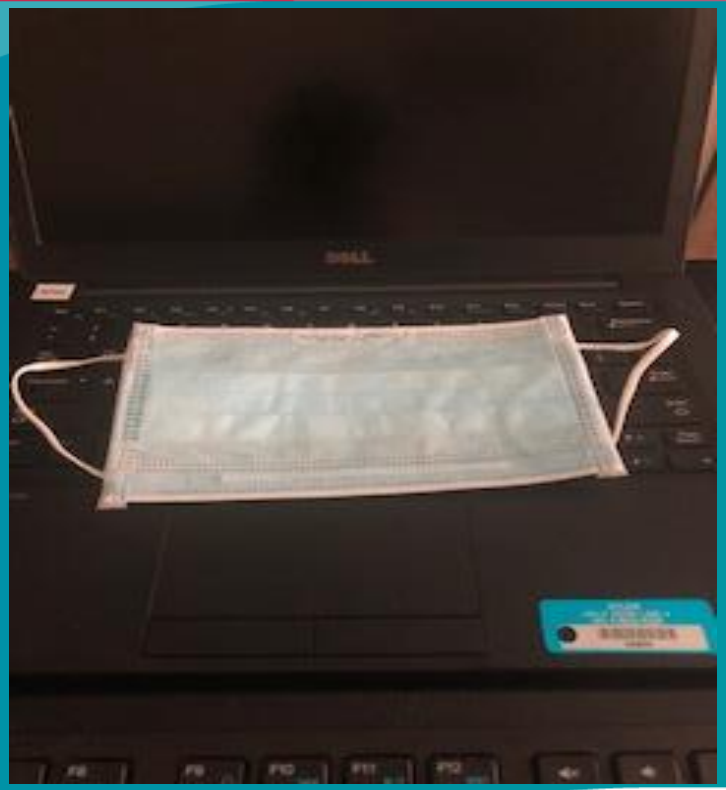
Types of Masks

1. Surgical Masks



The primary recommended medical function of this type of disposable mask is for ‘infected’ individuals to decrease the risks of transmitting viruses to other people in the vicinity

**It protects us but with some limitations:

- protects against large droplets of bodily fluids
- prone to leakage around the edges especially when inhaling
- Lower level of respiratory protection against smaller airborne particles

1. Surgical Masks

Must be considered as single-use disposable masks. They are made of:

- Non-woven fabric for better bacteria filtration
- Plastic (or metal) nose wire or lining
- Polypropylene for better filtration efficiency

These type cannot be decontaminated.

Safe and Reliable brands are made “Sterile” but Dry Heat Sterilization MUST NOT be used

High Temperatures will cause physical damage to the Surgical face mask

EtO Sterilization Procedures for Surgical Face Masks

Four (4) Phases of operation:
1. Pre-conditioning / Conditioning
2. Exposure (Sterilization)
3. Exhausting (Post-conditioning)
4. Purge (Pulling Vacuum)

Four (4) Primary Variables:
1. Gas Concentration (EtO)
2. Humidity (%RH)
3. Temperature
4. Time

EtO Sterilization

Ethylene oxide is a low temperature gaseous process widely used to sterilize a variety of healthcare products, such as single-use medical devices.
Through the use of a vacuum-based process, EtO sterilization can efficiently penetrate surfaces of most medical products and its lower temperature makes it an ideal process for a wide variety of materials such as the face masks.

By using EtO, materials are not exposed to excessive heat, moisture, or radiation.

"But EtO Processes requires regular Validation"

- Validate the 4 Phases
- Validate the 4 Variables

EtO Sterilization according to ISO 11135-1

- **Pre conditioning** – expose products to tropical environment for at least 12 hours at 55°C/70% RH.
- **Exposure** – pull vacuum and expose to gas usually for 4 to 8 hours (varies per product and must be validated).
- **Post conditioning** – air out and only the EtO gas. 8-12 hours

Temperature and RH% are critical in pre-conditioning to induce microbial activity

EtO will not kill many microbes in their dormant or (spore) stage.

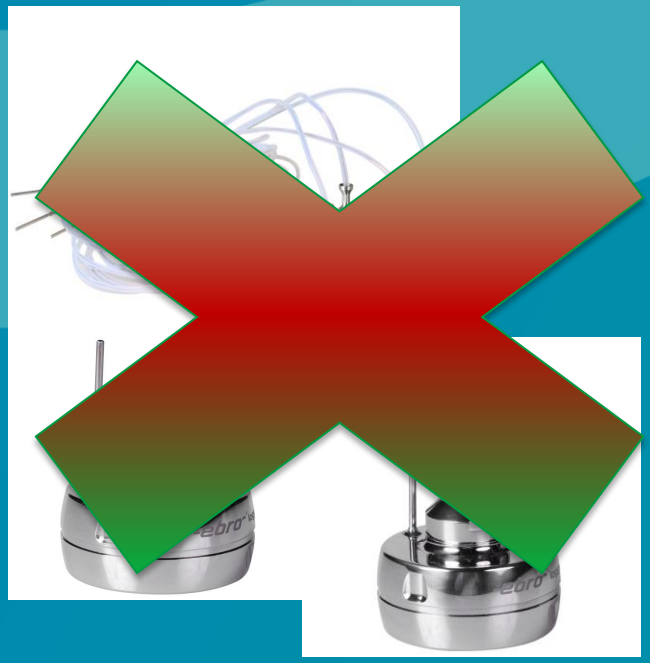
Moisture is critical as a transfer agent for EtO – it helps to permeate through plastic, paper, cardboard, packaging etc.

- **Purge -** Pulling a vacuum dramatically dries out the product. Therefore steam (RH) is increased to replace lost moisture in the product.

The influence of pressure is also a factor in helping EtO permeate a product.

…Pulling a vacuum pulls EtO into product.

Validation of EtO Sterilization cycles



Always check ATEX mark

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EtO Sterilization for other medical PPEs and devices:

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Types of Masks

2. N95 Masks

Far better than surgical face masks, the N95 respirator masks are sealed and tight-fitting and it forces all air through a filter which is designed to prevent more than 95% of 0.3microns of human droplets and particles

- Re-use is possible when necessary as it can be disinfected after use.
- Can be sterilized by EtO
- Contaminants and other viruses can also be inactivated by H_2O_2 Sterilization without damaging the N95 masks

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2. **N95 Masks** - *How they are made Sterile*

- **Steam Sterilization**; possible but causes degradation

- **EtO Sterilization**; for bulk sterilization of N95 masks takes longer process by nearly 2 days

- **H_2O_2 Sterilization;** the most effective sterilization method for N95 respiratory masks

H_2O_2 Sterilization causes no significant degradation to the respirator's filter even after 50 cycles were performed.

When validated with spores of geobacillus stearothermophillus, a 6-log reduction is achieved
(*same results produced by steam sterilizers)*

- ***Requires Validations !!!***

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2. **N95 Masks** – *as regulated FFRs*

- **Not approved for routine decontamination and reuse as standard of healthcare**

- **However, due to the COVID19 spread, FFR decontamination and reuse is now considered as a crisis capacity strategy to ensure continued availability of N95 respiratory masks**

- **H_2O_2 Sterilization** is highly recommended especially for used masks as all particulates blocked by the mask are all held inside it and therefore must be sterilized with H_2O_2 if it is not discarded.

**Mask Sterilization Protocols and Validation Protocols are available since 2016*

H_2O_2 Sterilization

Hydrogen peroxide sterilization, also known as hydrogen peroxide gas sterilization, used in Plasma Sterilizers, is a low temperature sterilization process commonly used to sterilize heat-sensitive devices.

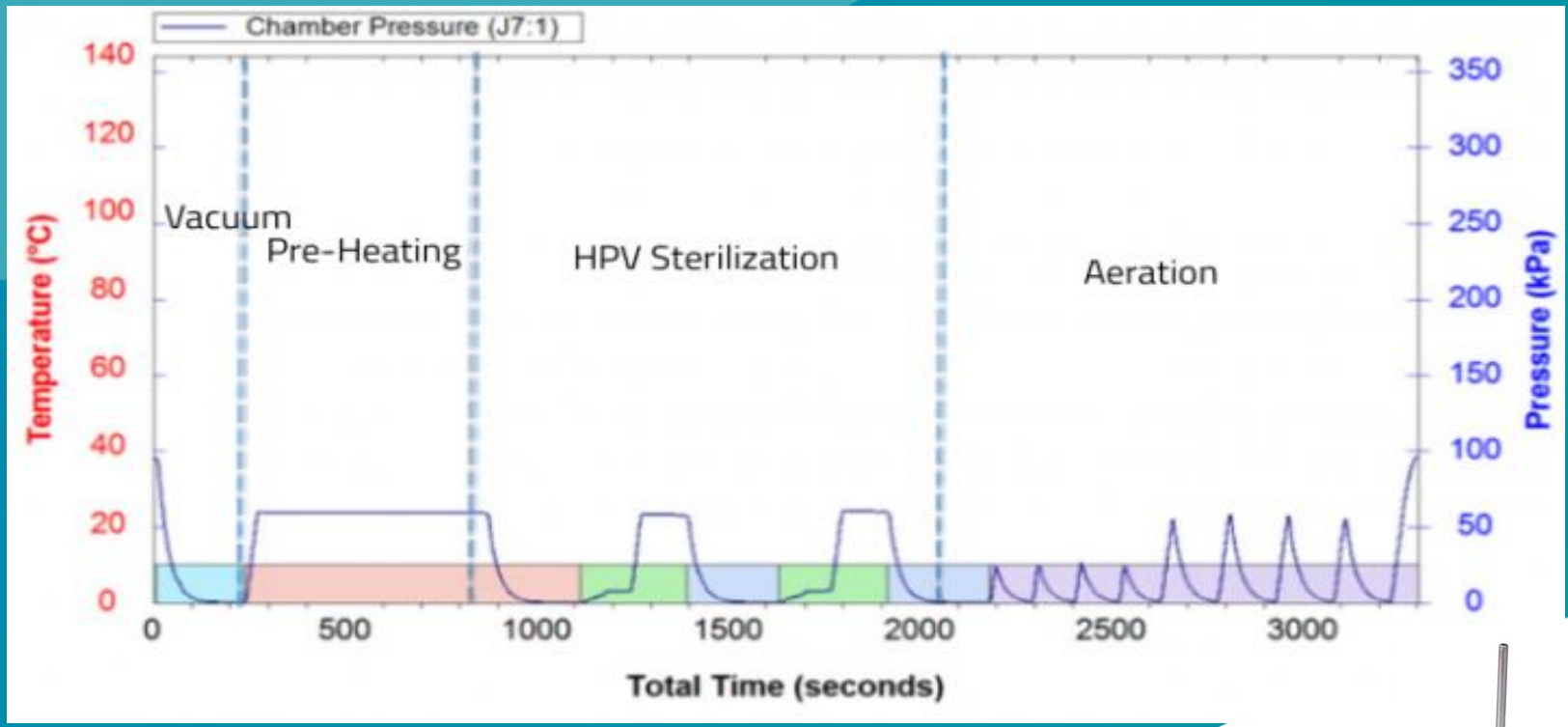
This sterilization process involves filling the sterilizer chamber with H_2O_2 vapor. Once the sterilization cycle is complete, the vapor is vacuumed from the chamber and converted to water and oxygen.

H_2O_2 Sterilization - Four Primary Stages:

1. Sterilization chamber pressure is reduced to a very high vacuum
2. Liquid H_2O_2 is converted into vapor
3. Under high vacuum, vapors fill the chamber, contacting all surfaces
4. After sterilization, the vapor is vacuumed from the chamber and converted into water and oxygen

With FFR Masks, the entire H_2O_2 process is carried-out in a constant temperature of 55.0°C

H_2O_2 Sterilization - Four Primary Stages must be verified:



The Challenge is to measure pressure down to **0.01 kPa**

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Hydrogen Peroxide Gas Plasma Sterilisation

The Plasma Phase. An electromagnetic field is created in which the hydrogen peroxide vapor breaks apart, producing a low temperature plasma cloud that contains ultrviolet light and free radicals.

The Vent Phase. The chamber is vented to equalize the pressure enabling the door to be opened. There is no need for aeration or cool-down. Devices are ready for immediate use.

Applications of Ebro Solutions

EBI 12-T441 Temperature
-200.0°C to +200.0°C

EBI 12 –TP290 Pressure
0.0°C to 85.0°C
0.1mbar to 1,050 mbar

Types of Masks

3. Elastomeric Respirator Masks

The most effective of the FFRs.

The Elastomeric Respirator Masks are Half-Facepiece and tight-fitting **respirators** that are made of synthetic or rubber material permitting them to be repeatedly disinfected, cleaned, and reused.

This type is equipped with exchangeable filter cartridges.

3. Elastomeric Respirator Masks

Cleaning and disinfection procedures including Sterilization methods can be from predetermined SOPs established by the users' own organization or offices.
This is due to the robustness in construction, rigidness in design and more stable materials that are used in this type of respirator and therefore even makes some of its components and filters to be sterilized in high temperatures such as in the steam sterilizers

Cleaning and disinfection are the most common methods used to decontaminate and make this FFR safe for reuse.

Types of Masks

3. Cloth Face Masks

The least effective of the face masks

A cloth face mask will not completely protect you from the virus. However, a cloth face mask, including those homemade masks, can provide light protection and remind you not to touch your face. It also helps prevent the spread of germs from the person wearing it to others.

It helps block large droplets from coughs and sneezes

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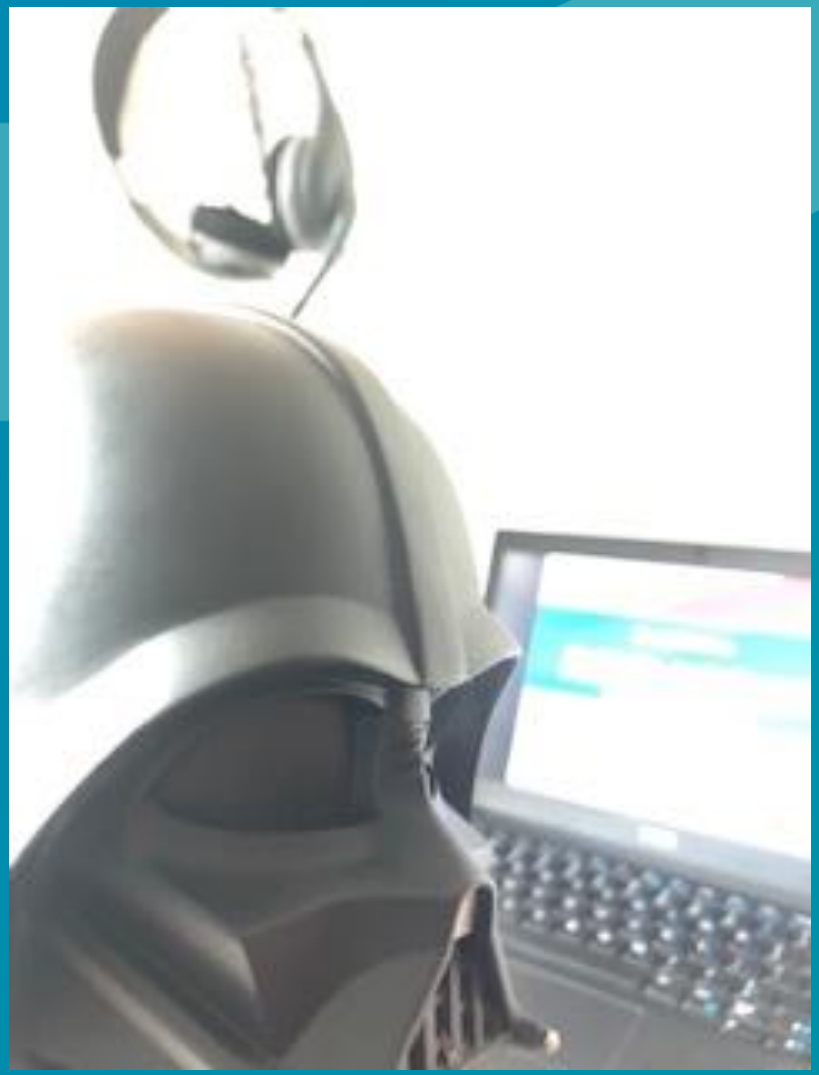

Please help inform all our customers using H_2O_2 and EtO Sterilizers that Xylem Analytics has the solutions for all their validation and qualification requirements with Ebro.

If they can't purchase just yet, they may rent the loggers or may avail of the Xylem Validation Services

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- **Q: Are we still on with our Session's Topic?**
  (talking about masks and how they are sterilized and disinfected?)
  "Practical Solutions for your Routine Monitoring and Validation Requirements" – Pharma / Healthcare

Answer: Yes

Other Pharmaceutical / Healthcare products, aside from FFRs, are processed in the same manner and is always guided by Standards and Norms & therefore performed with SOPs and Validation Protocols

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- **Disinfection and Sterilization Processes are, most often than not, always guided by Standards and Norms & therefore performed with SOPs and Validation Protocols**

And Xylem Analytics, our partners and teams of consultants, are available to help and assist you

- Thermal Process Validations
- Process Adequacy Determination and Establishment
- EtO and H2O2 Validations
- Provide Trainings for the above to cope up and not be limited by the Travel Restrictions

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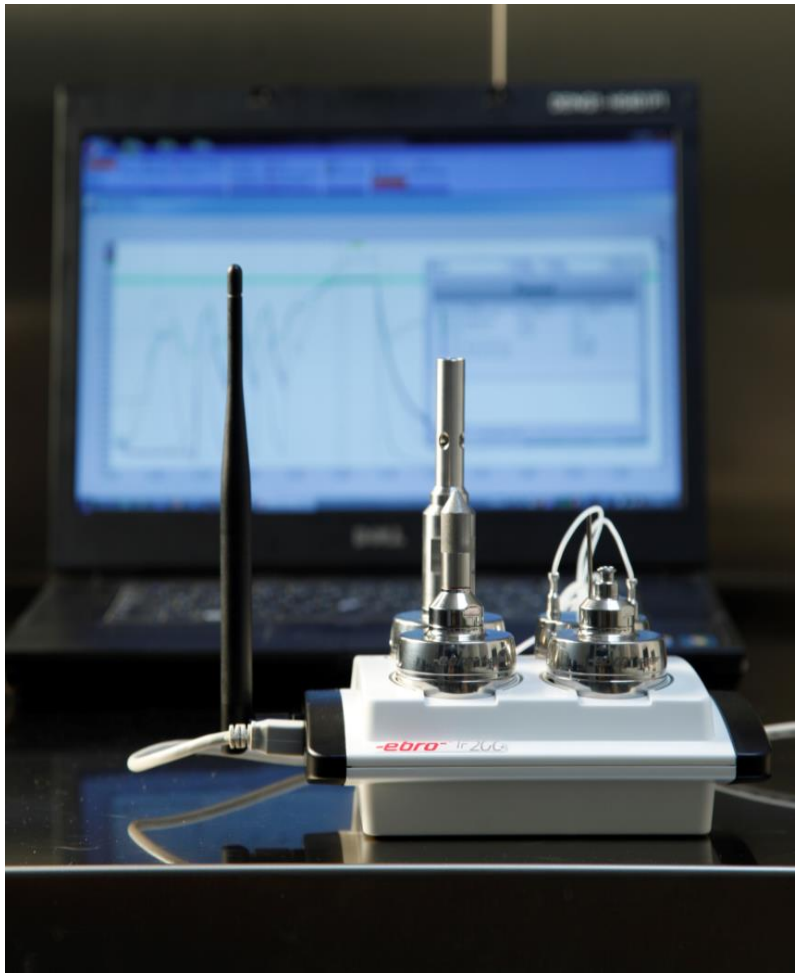
VALIDATION

The essentials of Validation: The **Installation Qualification (IQ)**, the **Operation Qualification (OQ**) and the **Performance Qualification (PQ).**

Validation is a complete presentation and verification of facts, that procedures, processes, equipment, materials, process steps or systems actually lead to the expected results.

The results are then **summarized** and presented in details in a **validation report**, which helps to evaluate and assess the predetermined acceptance criteria and process optimization objectives



Routine Control

Routine controls are series of periodic verifications to check if the operating performance of the sterilizer meets the limit values that were defined during the validations.

The frequency of performing routine controls depends on the machineries and the processes which is solely on the responsibility of the operator and the QC or Validation Manager.

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Validation of processes in steam sterilizers

Must be conducted or performed only by authorized personnel

Knowledgeable about the Regulations, the Standards and the Norms

Qualification

Installation Qualification (IQ)

- the washer-disinfector and its accessories are properly supplied and duly installed with the correct connections, fixtures and peripherals

Operation Qualification (OQ) ensures that

- the equipment of the washer-disinfector and the media supply comply with the manufacturer specifications as well as with the requirements of EN ISO 15883

Performance Qualification (PQ) comprises the thorough evaluation of the ff:

- Cleaning performance
- The adequate removal of process chemicals
- Adequacy of the disinfection process
- Evaluation of the Drying Process

Standards and Norms

- **EN ISO 17665** – Steam Sterilization - Validation and routine control of dry-saturated steam sterilization

  Sterilization of medical devices - Validation and routine control of sterilization by moist heat (DS EN ISO 17665-1)

- **EN ISO 11135** – EtO Sterilization of medical devices - Validation and routine control of ethylene oxide sterilization (DS EN ISO 11135-1)
- **EN ISO 14937** – Vaporized Hydrogen Peroxide Sterilization; H_2O_2

Low Temperature Sterilization Standard

- **DIN 12880/2** – Oven verification

- **DIN 58945/2** – Incubator verification

Provisions in the ISO 17665

ISO 17665 is kept very open.

ISO 17665 does not require compliance of the temperature band or plateau time. It must be verified that the required F0 value is reached in all positions under saturated steam conditions.

According to ISO 17665, also processes of older sterilizers that are not compliant to the standard EN 285, EN 13060 can be validated

An annual validation cannot specifically be explained, but typical annual re-qualification is necessary (ISO 17665-2 part 12.4). The time interval depends on the risk evaluation as well as the procedure stability.

Conclusion:

The requirements to the performance of the validation have increased. A high level of expertise is required in order to be able to perform a validation of a sterilization procedure technically correct.

Reaching the sterilization conditions

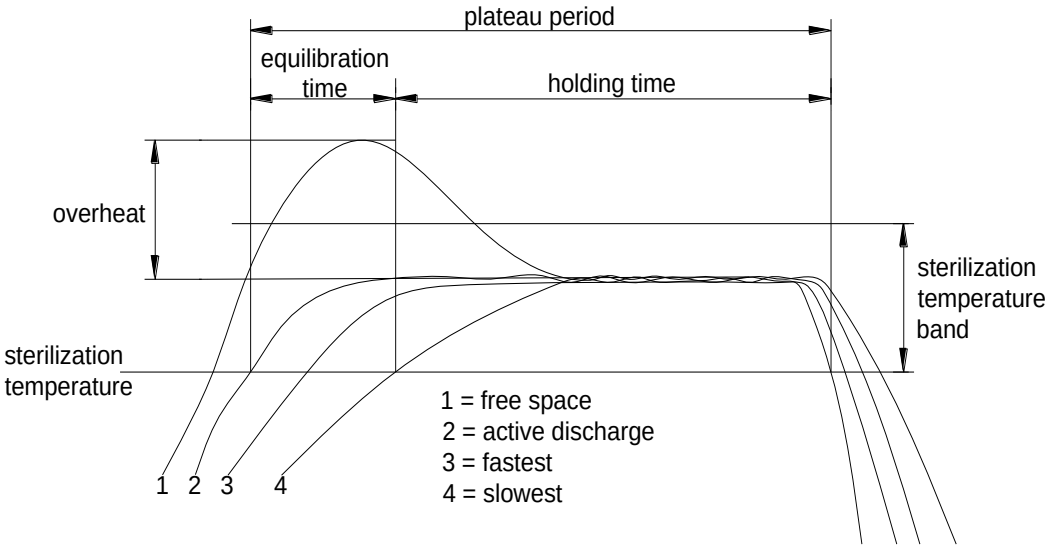
The existence of saturated steam in the usable area and within the loading can be considered as reached, if all temperatures measured in the usable area and within the loading during the hold time:

- are not below the sterilization temperature
- are not more than 3K (large sterilizer and small since 2016) / 4 K (small sterilizer before 2016) above the sterilization temperature
- do not diverge by more than 2°C
- equilibration time 15 s to 800 liter, 30 s for larger sterilizers
- minimum hold times 121 °C for 15 min; 126 °C for 10 min; 134 °C for 3 min
- F_0-Value minimum15 min

The saturated steam temperature that is calculated with the measured pressure is to be considered as measured temperature.

Interpretation of the thermometric measurement

The compensation time / equilibration time is the period of time between reaching the sterilization temperature in the sterilization chamber (reference measuring point in the coldest point) and reaching the sterilization temperature in all points of the loading. The equilibration time may not exceed 15 s for sterilizers up to 800 l or 30 s for larger sterilizers.



Measuring values outside the tolerances

What measures need to be taken in case the results do not correspond to the specifications?

1. Check if the loading is correct?
2. Positioning of the measuring sensors
3. Repeated calibration of the measuring system
4. Adjust process parameters by manufacturer or service company (e.g. confining / chamber pressure, pressure period)
5. Alternative medical products? (materials, construction)

SOP – Standard Operation Procedures

Operating instruction

Step-by-step instruction

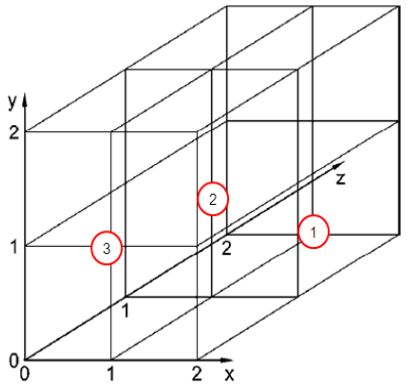
Explanations and examples for completing the paperwork

Advice for positioning of the sensors

Integration in the software Winlog.validation

Separate parts are explained(IQ, OQ, PQ)

- Revalidation
- Shortened validation



1: Referenzmessstelle
2: Mittig im Kammerinnenraum
3: In Türnähe

Validation of the thermal processes

Suitable data logger

EBI 12 pressure logger with rigid probe or flexible probes with luerlock

EBI 12 pressure logger with 1.5 mm flex probe with luerlock

EBI 11 and EBI 12 temperature logger with rigid and bendable probes

EBI 11 pressure logger with luerlock and without luerlock

Validation of the thermal process in Plasma sterilizers

Suitable temperature / pressure logger for measuring in Plasma sterilizer H_2O_2

- Low pressure and temperature logger
  EBI 12 TP 190
- Measurement range: 0 … +85°C
  0 … 1050mbar
- Accuracy: ±0,05°C
  ±0,25mbar
- Part number: 1340-6665
- Not suitable in steam sterilizer

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Software winlog.validation

We need you to Learn !

The only way we can all be successful and earn the industry's confidence on us
Is to be able to maximize and optimize the functionalities and capabilities of the Winlog.Validation Software.

Please contact Ebro or myself to arrange this and we will be happy to accommodate you.

Evaluation software Winlog. Validation

Software for validating sterilization processes as per EN ISO 17665 and pr DIN 58929

FDA 21 CFR Part 11 compliant software (needed in the pharmaceutical industry)

Validated by TÜV Munich

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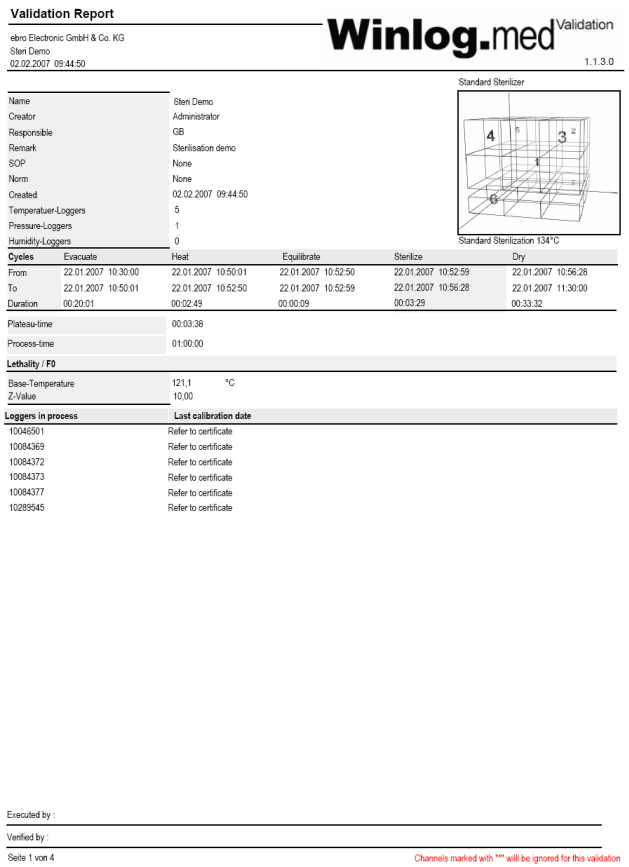
Validation report for sterilization processes



Validation Report

Winlog.med Validation 1.1.3.0

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Steri Demo
02.02.2007 09:44:50

Standard Sterilizer

Standard Sterilization 134°C

Name	Steri Demo
Creator	Administrator
Responsible	GB
Remark	Sterilisation demo
SOP	None
Norm	None
Created	02.02.2007 09:44:50
Temperatuer-Loggers	5
Pressure-Loggers	1
Humidity-Loggers	0

Cycles	Evacuate	Heat	Equilibrate	Sterilize	Dry
From	22.01.2007 10:30:00	22.01.2007 10:50:01	22.01.2007 10:52:50	22.01.2007 10:52:59	22.01.2007 10:56:28
To	22.01.2007 10:50:01	22.01.2007 10:52:50	22.01.2007 10:52:59	22.01.2007 10:56:28	22.01.2007 11:30:00
Duration	00:20:01	00:02:49	00:00:09	00:03:29	00:33:32

Plateau-time	00:03:38
Process-time	01:00:00

Lethality / F0

Base-Temperature	121,1 °C
Z-Value	10,00

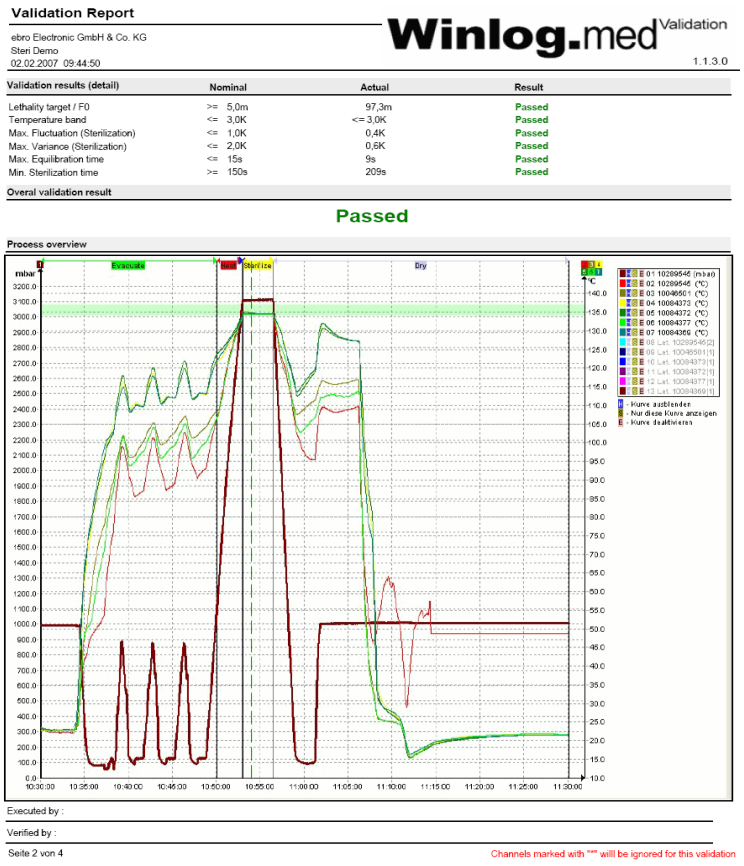
Loggers in process	Last calibration date
10046501	Refer to certificate
10084369	Refer to certificate
10084372	Refer to certificate
10084373	Refer to certificate
10084377	Refer to certificate
10289545	Refer to certificate

Executed by :

Verified by :

Seite 1 von 4

Channels marked with "*" will be ignored for this validation



Validation Report

Winlog.med Validation 1.1.3.0

ebro Electronic GmbH & Co. KG
Steri Demo
02.02.2007 09:44:50

Validation results (detail)	Nominal	Actual	Result
Lethality target / F0	>= 5,0m	97,3m	Passed
Temperature band	<= 3,0K	<= 3,0K	Passed
Max. Fluctuation (Sterilization)	<= 1,0K	0,4K	Passed
Max. Variance (Sterilization)	<= 2,0K	0,6K	Passed
Max. Equilibration time	<= 15s	9s	Passed
Min. Sterilization time	>= 150s	209s	Passed

Overal validation result

Passed

Process overview

Executed by :

Verified by :

Seite 2 von 4

Channels marked with "*" willl be ignored for this validation

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7 April 2020

Thank you!

Feel free to contact us

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