

Ebro Webinar Session P.4: Process Qualifications & Validations in Food, Pharmaceutical & Medical Industries



What to Expect in this Session:

- Brush up on the previous Webinar Sessions
- Brief introduction of all Ebro Products
- Ebro as essential tool for Audit and Regulatory Compliance
- Ebro as a Solution for Validation Requirements
- Food Applications
- Pharmaceutical Applications
- Medical Segment of Industry: What Makes Ebro a Total Solution for the SOPs and Standards in the Hospitals
- Ebro beyond the definition of ***“Data Loggers”***

What we can arrange and organize *virtually* in the coming weeks:

- Software Trainings: Separate sessions for different **Winlog** Software Packages
- Polishing up on our knowledge with important applications: Multi-Industry
 - *How to effectively introduce our solutions*
- Trainings on Food Processes: Thermal Processing Methods
- Thermal Process Validations in the Pharmaceutical industry
- Addressing the CSSD Requirements: We need to know more about this important opportunity in the Hospital / Medical institutions

*****The webinars are only 1-hour sessions and therefore presents the important information about the Ebro Solutions***

******We need longer time for the above and it is highly recommended they are organized separately with interested business partners and customers.***

*******We encourage everyone to have their own loggers and software to make this a successful learning process***

Thank you and keep well, mentally, physically and spiritually





























Our sincerest appreciation of your time especially to those who have been with us since we started these 4-series of Ebro Webinars.

“While this COVID19 knows no alliance and respects no boundaries to create such an immensely damaging impact to the world; it continues to fail in causing us to lose our conviction and hope... and so therefore life goes on”

- AJ

Xylem:

Bringing together the most progressive brands

Transport	Treatment	Dewatering	Applied Water Solutions		Measurement & Control Solutions		
 	   	  	     	<p>Specialty Flow Control</p>   	 	<p>Analytics</p>           	<p>Advanced Infrastructure Analytics</p>       

1st Webinar session

BULK SUPPLY

General Store

Clean Receipt

Wards & Units

Dirty Receipt

OPERATING THEATER PATIENT ROOMS

Cotton,
Gauze, etc.

Disassembly

Washer + Disinfectors

Instruments

Gloves



Rubberwares

Assembly

Inspection

Pre-Sterile Storage



Sterilization

Sterile Storage

Distribution

2nd Webinar session

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



- *Decontamination and Sterilization Methods
For PPEs and FFRs*

EtO Sterilizers, H2O2 Sterilizers and
Steam Sterilizers

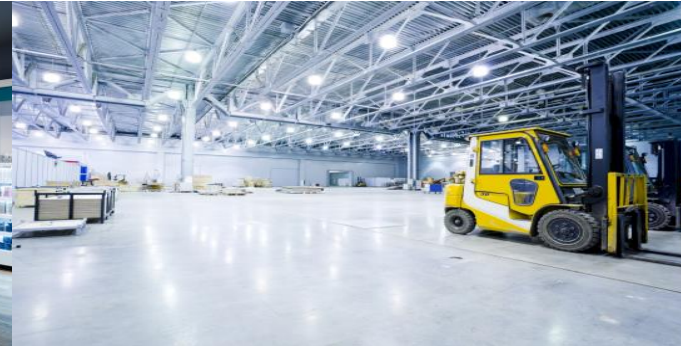
3rd Webinar Session

Cold Chain Monitoring (Cool Chain)

Requirements for Temperature and Humidity Records to accurately document product transport conditions and must capture possible negative impacts on the goods.

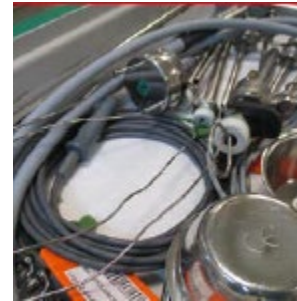
Destinations and recipients includes:

- Hospitals
- Pharmacies / Drug Stores
- Resident Doctors
- Warehouses



Ebro Product Classifications:

Process Monitoring, Routine Control and Validation



Ebro Product Classifications:

Process Monitoring, Routine Control and Validation

Storage Mapping Applications

Refrigerators/Fridges and Stability Cabinets/Stability Rooms



Ebro Product Classifications:

Other Applications

Food & beverages



- Logistics / Storage
- Transport
- Vacuum Measurements / Headspace Establishment
- HDT and HPT
- Food Oil Quality
- Process Schedule Verification
- Freezing Methods

Medical & Pharmacy



- Logistics / Storage
- Transport
- Sterilization
- EtO Sterilization
- H₂O₂ Sterilization
- Depyrogenation
- Lyophilization
- Freeze Drying

Industrial



- General
- Incubators
- Clean rooms
- Mapping



Qualifications and Validations:

The Ebro Approach

Qualifications and Validations:

Please Note the following Products that will be used for the Applications that will be mentioned in the succeeding slides



EBI 11 Series



EBI 12 Series



EBI 16



EBI 310 Series



EBI 25 Series



TRACEbro 310



VAM 320-EX Vacuometer

What is Qualification and Validation?

The same in Food, Pharmaceutical and Medical

Qualification Stages:

- IQ - Installation Qualification

The Performance of documented verification that an equipment/system installation adheres to approved contract specifications and achieves design criteria. This establishes documentary evidence that an equipment is installed in compliance with technical specifications, standards, codes and regulations

- OQ - Operational Qualification

The documented verification that an equipment/system performs per design criteria over all defined operating ranges. This establishes documentary evidence that an equipment is capable of repeated operation within the limits defined in the specifications.

- PQ - Performance Qualification >> What we typically call “Validation”

Documented verification that equipment or processes operate the way they are purported to function. Critical parameters (temperature, pressure, conductivity, humidity, etc) must be stable over time and under both normal and worst-case conditions.

Qualification Stages According to Requirement Classifications and User Specifications in all Key Industries such as the ff:

Industrial: Refrigerators, magnetic stirrers

F&B: Logistics

F&B: Food retail

F&B: Food services

F&B: Oil quality

F&B: Processing

Medical: Blood banks / Plasma
Hospital routine control / CSSD

Pharma: distribution

Pharma: manufacturing

Pharma: logistics

Partner Logos: CONRAD, DACHSER Intelligent Logistics, TNT, Kaufland, REWE, LIDL, EDEKA, Miele, GETINGE GETINGE GROUP, MMM Group, pluradent, HENRY SCHEIN®, VWR, LLG Lab Logistics Group, Fisher Scientific Part of Thermo Fisher Scientific, Alcon CIBA VISION, BASF We create chemistry, gsk, Nestlé, Burger King, McDonald's, Quick, KFC, Manitowoc, Rasthofen, BAYER.

What is Qualification and Validation?

Relatively the same in Food, Pharmaceutical and Medical

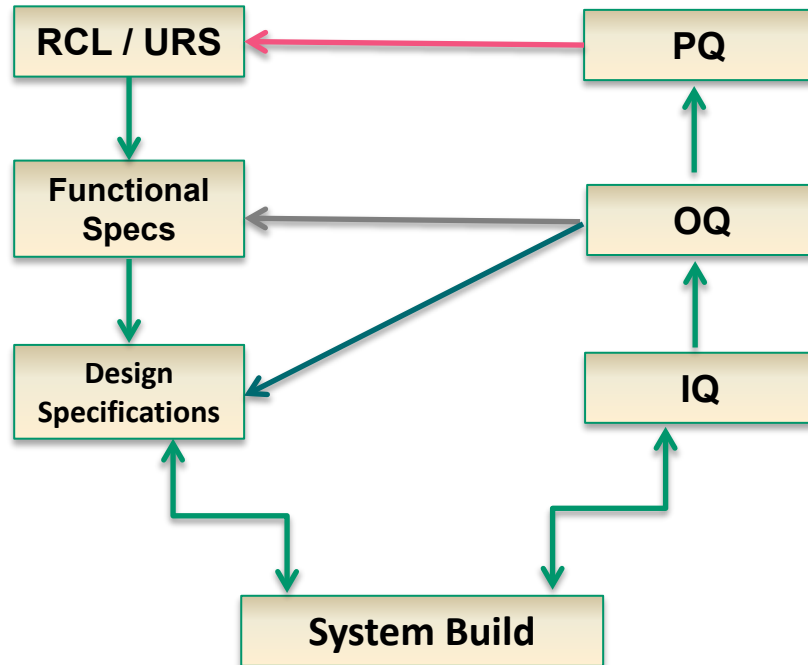
Validation (Europe and the USA)



Establishing documented evidence which provide a high degree of assurance that a specific process will consistently produce a product meeting its pre-determined specifications and quality attributes.



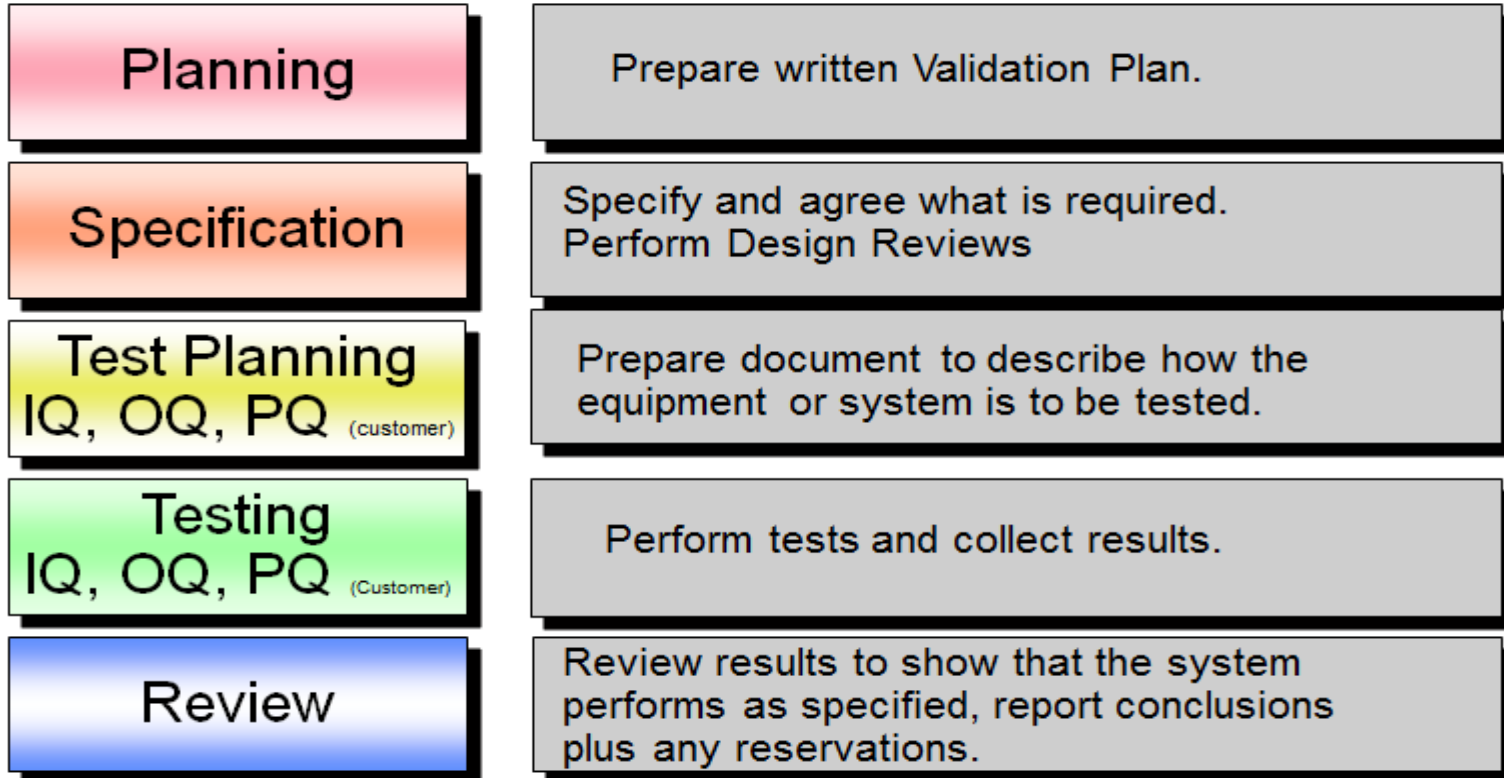
Action of providing, in accordance with the principles of Good Manufacturing Practice, that any procedure, process, equipment, activity or system actually leads to the expected results.



What is Qualification and Validation?

The same in Food, Pharmaceutical and Medical

Qualification / Validation Flow



”Action of providing, in accordance with the principles of Good Manufacturing Practice, that any procedure, process, equipment, activity or system actually leads to the expected results.”

...expected results:

1. Microbial Inactivation

- Commercial Sterility – Packed or Canned food products that have been sufficiently heat-processed and properly handled and stored, turning heat-resistant microorganisms and non-toxic thermophilic spore-formers to remain dormant and therefore will not present any health risks to the consumer.

2. Good Quality

- Criteria on Desired Sensory Attributes – Not over-cooked; desirable color, odor, texture and taste
- Criteria on Safety without compromising on desired Food Nutrients

Ebro Approach – EBI 11 and EBI 12 Wireless Data Loggers with the Winlog.Pro Software for Lethality Calculations, e.g. F_0 -value / P_u -value Calculations and even C_0 -value Calculations

Thermal Processes in the Food Industry

What you measure before the implementation of the Thermal Processing Methods:

1. Vacuum

- A measure of the extent to which air has been removed from the container. Less air in the container after sealing is an indication of a strong vacuum which is necessary for thermal treatment.
- Air Molecules inside the packaging can build up the pressure during thermal processes and can exert a lot of pressure on the lid and seams of the container

It is an SOP to measure the Vacuum in Packed Foods in all Canning Operations Before any Heat Treatment or Thermal process

What is normally used here by the industry is a Dial-Type Vacuumeter

- The Ebro Approach is with the more reliable VAM 320 Digital Vacuum Meter



VAM 320-EX Vacuumeter

Food Industry

Regulated Processes

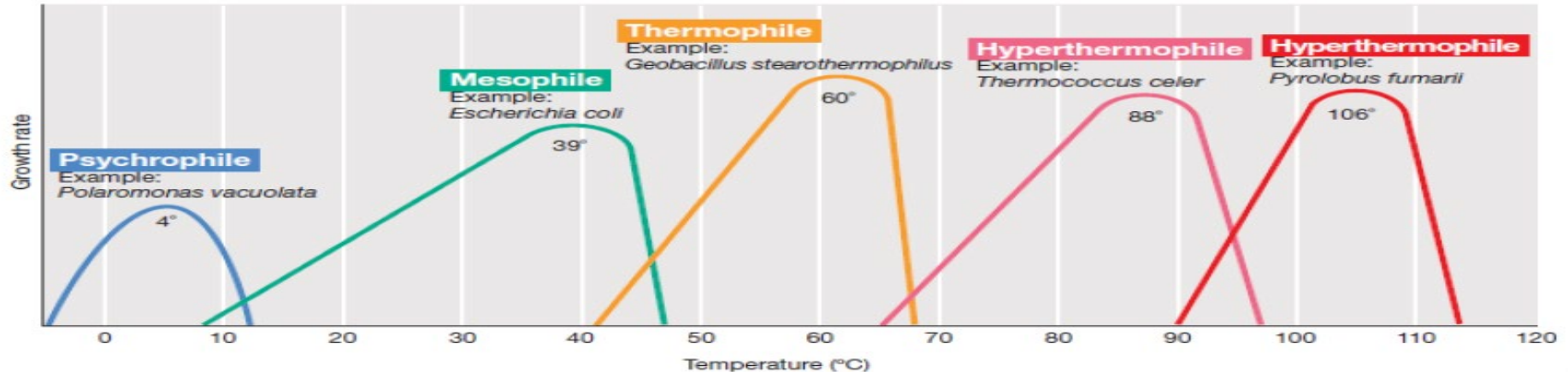
Thermal Processes in the Food Industry

What you measure before and after the implementation of the Thermal Processing Methods:

2. Initial and Final Temperatures of the Products

- Initial Temperature or IT of the products before any Heat Treatment or Thermal Processes or Freezing
- Post-Process Initial Temperatures of the Finished Food Products before they are cooled or Frozen or Stored

One of the Important Objectives of Cooling is to prevent Microbial Re-growth



Food Industry

Regulated Processes

Thermal Processes in the Food Industry

What you measure before and after the implementation of the Thermal Processing Methods:

2. Initial and Final Temperatures of the Products

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1st and/or last container or from random sampling



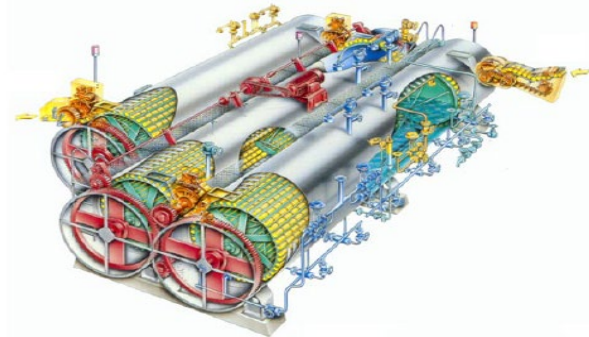
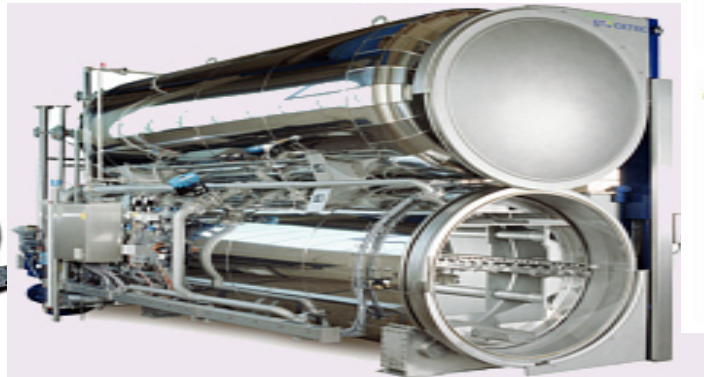
Continuous Measurements from Heat Treatment to Cooling

Thermal Processes in the Food Industry – How We Validate

I. DATA ACQUISITION from Different Thermal Processing Methods:

1. Retorting (Sterilization)

- By performing Heat Distribution Tests (**HDT**) in the retort following the acceptable Guidelines
- Conducting Process Adequacy Determination to establish acceptable and safe process schedules via Heat Penetration Tests or **HPT**
- Evaluating over-all adequacy of the retort process against all pre-determined criteria on Food Safety and Regulatory Compliance



Thermal Processes in the Food Industry – How We Validate

1. Retorting (Sterilization) – Establishment of Acceptable Process Schedules for Different Container/Can Dimensions



Food Industry

Regulated Processes

Thermal Processes in the Food Industry – How We Validate

- 1. Retorting (Sterilization) – The EBI 11 for Process Adequacy Establishment by HPT for New Product Developments**
- Have you ever seen or heard of „Ducks“ with Cornish in Cans?



Thermal Processes in the Food Industry – How We Validate

1. Retorting (Sterilization) – or Mr. Ebro's Favorite „Shrimps“ in Cans?



Food Industry

Regulated Processes

Thermal Processes in the Food Industry – How We Validate

- 1. Retorting (Sterilization)** – *These mentioned Food Products are so Heat-Sensitive therefore requiring that Processes are measured correctly, and making HPT studies necessary to attain Food Safety and not Compromising on Quality.*



Not doing so could result to undesirable over-processed and poor quality Food products



Food Industry

Regulated Processes

Thermal Processes in the Food Industry – How We Validate

Aside from the advantage of using PT1000 sensor elements in the EBI 11 and EBI 12 Validation Loggers over Thermocouples that are prone to drifts, another advantage is...



The EBI 11s and EBI 12s, being Wireless,
No longer requires you to guide wires/cables
From outside to inside of the retort vessels

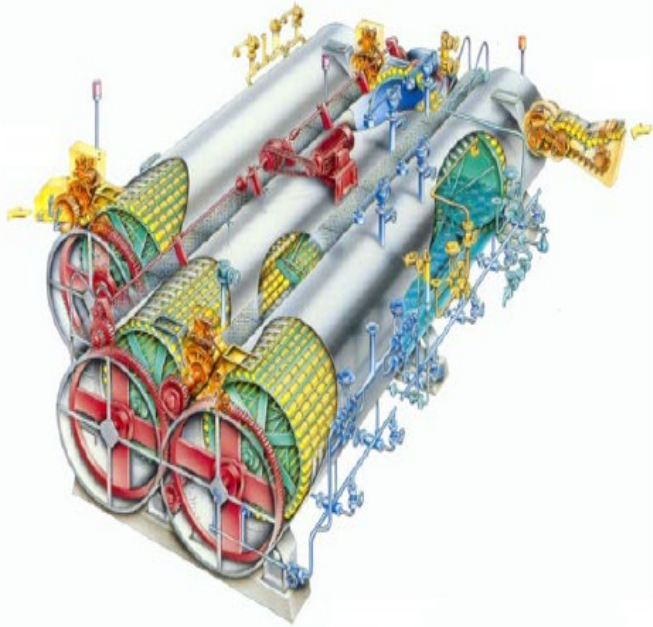


Food Industry

Regulated Processes

Thermal Processes in the Food Industry – How We Validate

And you do not want to do this, positioning the cables & thermocouple wires inside the Spiral-Cooker-Cooler

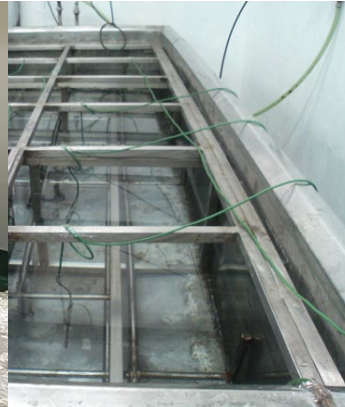


Thermal Processes in the Food Industry – How We Validate

Different Thermal Processing Methods:

2. Pasteurizers (Many Types)

- By performing Heat Distribution Tests (HDT) in the Pasteurizer Unit
- Conducting Process Adequacy Determination to establish acceptable and safe process schedules via Heat Penetration Tests or HPT
- Evaluating over-all adequacy of the Pasteurization process against all pre-determined criteria on Food Safety and Regulatory Compliance



Food Industry

Regulated Processes

Thermal Processes in the Food Industry – How We Validate

Different Thermal Processing Methods:

2. Pasteurizers

Pasteurization is typically implemented for acid and acidified food products like fruit beverages, etc.

However, some low-acid food products that are highly sensitive to high temperatures are also pasteurized

Examples of this Low-acid Food products are Milk, Creams and high-value foods such as abalone and crab meat



Food Industry

Regulated Processes

Thermal Processes in the Food Industry – How We Validate

Different Thermal Processing Methods:

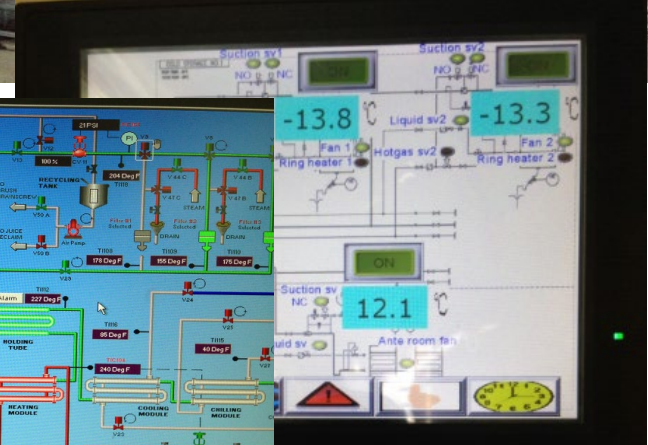
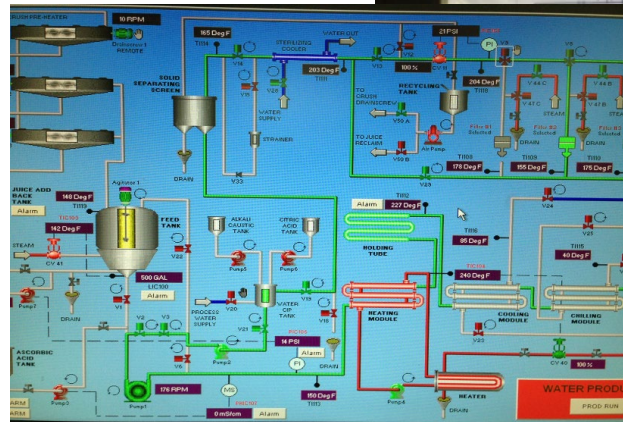
3. Hot-Fill-Hold Processing Methods

4. UHT-Aseptic Process

5. Sous-Vide Process (Cook-Chill)

6. Freezing

- IQF
- Blast Freezing
- Ethanol Freezing
- others



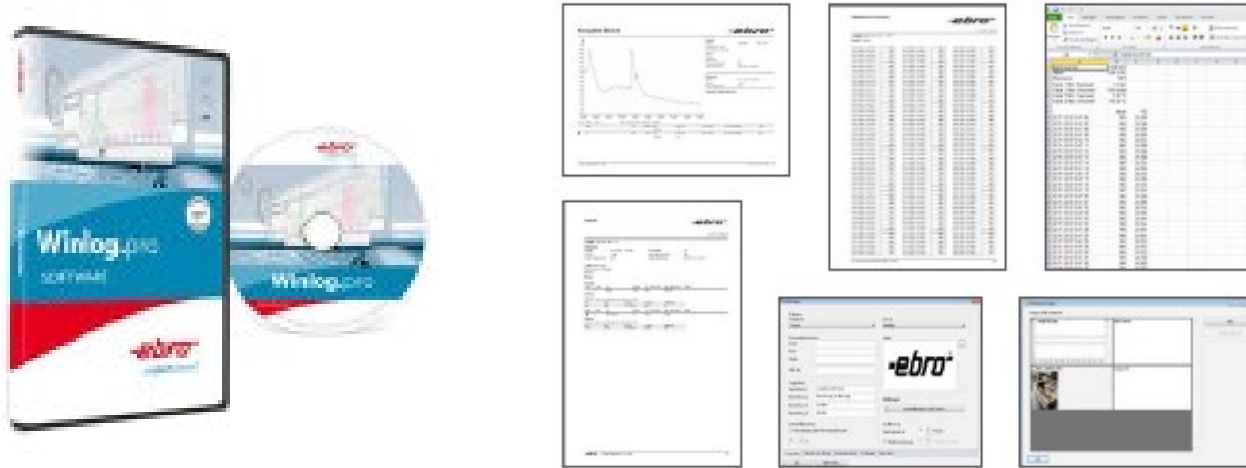
Food Industry

Regulated Processes

Thermal Processes in the Food Industry – How We Validate

II. Data Evaluation

- **Report Generations from the Parametric Measurements**
- **Lethality Value Calculations: Fo-value, Po/Pu-values, Co-values**
- **Process Deviation Reports / Statistics Report**



- ***In Food Applications – Know your Target Microorganisms !!!***

Food Industry

Regulated Processes

Thermal Processes in the Food Industry – How We Validate

- ***In Food Applications – Know your Target Microorganisms !!!***

HEAT RESISTANCE FOR SOME SPORE-FORMING BACTERIA USED AS A BASIS FOR HEAT STERILIZATION PROCESSES FOR LOW ACID FOODS

BACTERIA GROUPS	APPROXIMATE RANGE OF HEAT RESISTANCE	
	D	z
Low Acid and Semi-acid foods (pH above 4.5) Thermophiles (spores) Flat Sour Group Gaseous Spoilage Sulfide Stinkers Mesophiles Putrefactive anaerobes <i>C. botulinum</i> <i>C. sporogenes</i>	D ₂₅₀ 4.0 – 5.0 3.0 – 4.0 2.0 – 3.0 0.1 – 0.2 0.1 – 1.5	14 – 22 16 – 22 16 – 22 14 – 18 14 – 18
Acid Foods (pH 4.0-4.5) Thermophiles (spores) <u><i>B. coagulans</i></u> Mesophiles (spores) <u><i>B. polymyxa</i></u> and <u><i>B. macerans</i></u> <u>Butyric anaerobes</u>	0.1 – 0.07 D ₁₂₁ 0.1 – 0.5 0.1 – 0.5	14 – 18 12 – 16 12 – 16
High acid Foods (pH 4.0 and below) Mesophilic non-spore forming bacteria <i>Lactobacillus spp.</i> , <i>Leuconostoc spp.</i> , and yeasts and molds	D ₁₅₀ 0.5 – 1.0	8 – 10

Food Industry

Regulated Processes

Thermal Processes in the Food Industry

...as there are simply too many things to talk about the highly-diversified Food Processes in our industry today, I will be more than happy to sit down with you in the near future or you may call on me anytime you feel like talking about the ebro approach and how we can be of help towards your thermal process requirements.



Pharmaceutical and Medical

Legal and normative basics

Laws - Germany

Contain basic demands on the manufacturing of medicine.

The use of GMP demands is implemented in other formalities/guideline

- Medicines act
- Medicine and active ingredient manufacturing regulation
 - Ordinance of the medicine act
 - implements the principles and guidelines of the EU, that were defined in the EU-GMP guideline
- For medical products
 - medical devices act
 - medical device directive
 - medical device operator regulation

Legal and normative basics

Laws - USA

Code of Federal Regulations (CFR)

- Includes in 21 CFR 210 & 211 cGMPs for pharmaceuticals
cGMP rules = current GMP



Legal and normative basics

dispensatories



The European Pharmacopoeia provides common quality standards throughout the pharmaceutical industry in Europe to control the quality of medicines, and the substances used to manufacture them.

It is a published collection of monographs which describe both the individual and general quality standards for ingredients, dosage forms, and methods of analysis for medicines.

The European Pharmacopoeia has a legally binding character. It is used as an official reference to serve public health, and is part of the regulatory requirements for obtaining a Marketing Authorisation Application (MAA) for a medicinal (human or veterinary) product.

steam sterilization

- DIN EN 285 large steam sterilizers
- EN 13060 small steam sterilizers (< 60 liter)
- EN ISO 17665 validation of sterilizer processes
- DIN 58929 validation of small steam sterilizer processes
- ISO EN 11140-4 routine monitoring (Bowie Dick Test)

Legal and normative basics

standards

hot air sterilization

ISO 20857 requirements for the development, validation and routine control of a dry heat sterilization process

hydrogen peroxide sterilization

ISO 14937 requirements for characterization of a sterilizing agent and the development, validation and routine control of a sterilization process for medical device

Legal and normative basics

standards

- **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; H₂O₂
Low Temperature Sterilization Standard
- **DIN 12880/2** – Oven verification
- **DIN 58945/2** – Incubator verification

Validation

Each phase of the validation must be performed according to a documented procedure. It must be verified that every object used during the validation meets its specification. All changes of the product, the equipment or the sterilization procedure that are done during the validation need to be documented and justified. The validation of the proposed periodic controls must be verified.

The validation consists of the Installation Qualification (IQ), Operation Qualification (OQ), Performance Qualification (PQ) as well as the control and confirmation of the validation.

The Sterilization Process

Sterilization

Microbial Basics

Sterilization describes the procedure, that eliminates, removes, kills, or deactivates all forms of life and other biological agents on materials and objects

Medical

- Important for the preparation is an effective pre-cleaning (pH >10 and 55°C) with subsequent steam sterilization at 134°C for 5 minutes or 134°C for 20 minutes if the pre-cleaning is not possible
- Spores are generated by lower creatures like bacteria, fungi, protozoan and so on
- Endospores of bacteria are of importance, because they are highly resistant against dehydration, toxic and other aggressive substances, aging and heat
- A few bacterial endospores can resist some hours in cooking water and about one hour in dry condition at 150°C
- They can get killed in steam sterilizers at 121°C and 2bar for 20 minutes

Sterilization

Microbial Basics

Sterilization describes the procedure, that eliminates, removes, kills, or deactivates all forms of life and other biological agents on materials and objects

Medical

The target is, to ensure, that medical and surgical instruments do not transmit infectious pathogens to patients.

They need to be sterile, before they get in contact with the patients.

Sterility is measured by probability expressed as sterility assurance level (SAL).

It is generally accepted that a sterility assurance level (SAL) of 10^{-6} is appropriate for items intended to come into contact with compromised tissue, which has lost the integrity of natural body barriers.

A SAL of 10^{-6} means that there is less than or equal to one chance in a million that a particular item is contaminated or unsterile following a sterilization process.

Sterilization

Microbial Basics

Sterilization describes the procedure, that eliminates, removes, kills, or deactivates all forms of life and other biological agents on materials and objects

Medical

- The D-value can be used, to calculate the F-value
- The F-value is the sum of all lethal effects, that affect the microorganism population
- An F-value of 1 describes the aborticide effect of 121,1°C within one minute, depending on the z-value, which is specific for different microorganisms
- The z-value says by which amount the temperature has to be increased, to decrease the D-value to one-tenth
- It can be calculated: *Automatically by **Using the Winlog.validation** following the standard formula as follows:*

$$F_0 = \Delta t \sum 10^{\frac{T-121.1}{z}}$$

$$z = \frac{T_1 - T_2}{\lg D_2 - \lg D_1}$$

Sterilization

Microbial Basics

Sterilization describes the procedure, that eliminates, removes, kills, or deactivates all forms of life and other biological agents on materials and objects

Pharmaceutical

- Everything is Sterilized, from unfilled containers to Products and their final packaging
- All Sterilization Equipment or Machineries, Lab-Scale and Production-Scale Autoclaves need to be validated
- Procedures are guided by Published Guidelines and Standards, written and presented in a form of a Validation Protocol



Sterilizer types

accredited sterilization procedures

steam



hot air



ethylene oxide



hydrogen peroxide

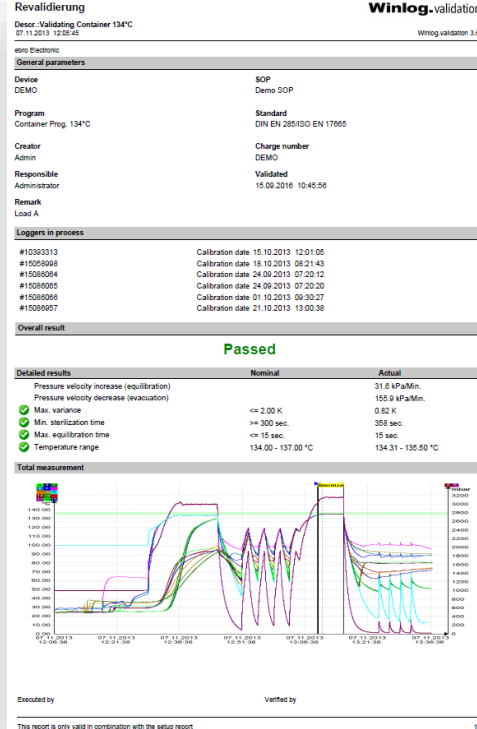
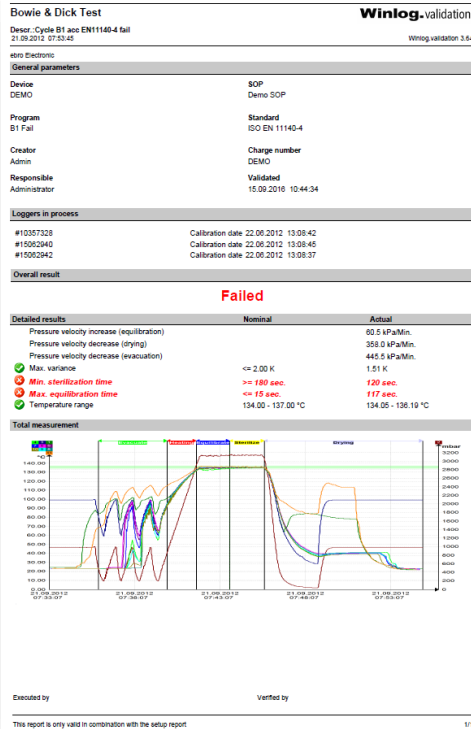


formaldehyde



Steam sterilization

process control – test equipment – ebro data logger solutions



Winlog.Validation automatically generates the PDF report

The PDF report includes:

- Status (Passed/Failed)
- Diagram for every phase
- Required parameters
- Measured parameters
- Calibration status of the logger
- Measurement table

Pharmaceutical Requirements

Regulated and for Strict Compliance

There are certainly a lot more important applications to discuss in the Pharmaceutical and Medical Segment of the Industry
– We will be happy to share more information about those topics that we are not able to present during this webinar due to limited time.

But remember that Ebro-Xylem and its people will always have the solutions for you.

Talk to you soon.

Thank you!

Feel free to contact us

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