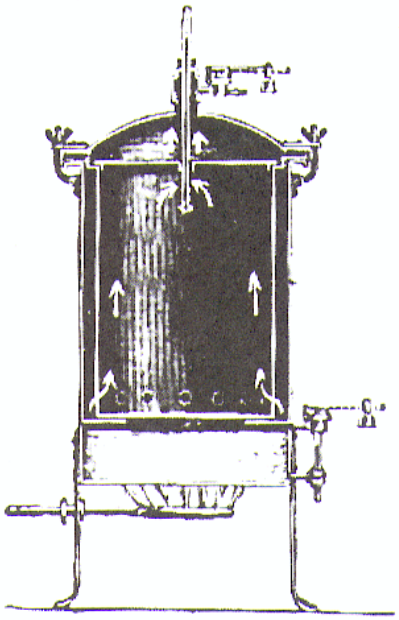
WFHSS ÖGSV

Sterile Supply Specialist Training Course Level I I



STERILIZATION OF MEDICAL DEVICES

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TABLE OF CONTENTS

Sterilization of Medical Devices

1 Definitions

Based on the definitions of international standards (the definition in brackets is the trial of a more understandable wording).

Sterilization: Validated process used to render a product free from viable microorganisms

(killing or irreversible damage of all viable microorganisms)

Sterile: condition of a medical device that is free from viable microorganisms

(with a probability of 1: 1,000,000)

D-value: Exposure time required under a defined set of conditions to cause a 1-logarithm or 90 % reduction in the population of a particular microorganism

(the D value (decimal reduction time) is the time in minutes that is required to reduce a population of a particular microorganism by one log level, corresponding to an inactivation rate of 90 %).

z value: Change in temperature in Kelvin (K) required to achieve a tenfold change in the rate of microbial inactivation by a moist heat disinfection process

(the z value gives the change in temperature in °C needed to cause a 10-fold change in the D value of an organism. z denotes the relationship between temperature and microbial inactivation and this is expressed in Kelvin (K) or °C).

SAL: Sterility **A**ssurance **L**evel expressed as the probability of survival of a microorganism after exposure to a sterilization process. Usually an SAL of 1: 1,000,000 (10^{-6}) is required.

Spores: Survival form of certain bacterial species (spore forming bacteria).

Steam: Gaseous water

Steam under pressure: Steam under a pressure that is higher than the atmospheric pressure (> 1 bar).

Saturated steam: Water vapour in a state of equilibrium between condensation and evaporation (Steam with maximum water content)

Superheated steam: Water vapour whose temperature is higher than the boiling point of water at the corresponding pressure

Autoclave: = Steam sterilizer, but this term usually is not used for sterilizers for medical devices (laboratory or waste autoclave).

Equilibration time: period which elapses between the attainment of the sterilization temperature at the reference measurement point and the attainment of the sterilization temperature at all points within the load

Sterilization module: rectangular parallelepiped of dimensions 300 mm (height) × 600 mm (length) x 300 mm (width). (Hence one StU has a volume of 54 litres.)

Standard test pack: Laundry pack comprising cotton towels measuring 22 x 30 x 25 cm as per EN 285.

BD test: Bowie & Dick Test

Non-condensable gas: Air and other gas which will not condense under the conditions of steam sterilization

Absolute temperature: Temperature scale which is based on the absolute zero point (0,00 K= -273,15 °C) (Usually a temperature difference is given in K).

Sterile barrier system: The minimum packaging configuration that provides a microbial barrier and allows aseptic presentation of the product unit at the point of use.

Batch: Quantity of goods or material produced in a single manufacturing run.

(In this context the term “batch” denotes the entirety (collectivity) of sterile supplies assembled in one sterilizer load, which is exposed to the same conditions and for which the same sterilization outcome can thus be expected.)

Validation: Documented procedure for obtaining, recording and interpreting the results required to establish that a process will consistently yield product complying with predetermined specifications.

(In this context Validation serves to furnish documented proof of the ongoing effectiveness of the reprocessing procedure under the operating conditions prevailing at the installation site, using the items encountered in routine operation in their respective packaging and with the reference loads used” (i.e. produces clean, disinfected or sterile devices).

Routine control: Tests to be carried out by the user to guarantee the ongoing effectiveness and reproducibility of the reprocessing procedures.

2 Introduction

Medical devices that penetrate the skin or mucosa, come into contact with wounds or are used for blood, blood products and other sterile medicinal products must be sterile when used (these are medical devices classified as critical by as per the regulations of the Robert Koch Institute - RKI).

However, that an object is free of viable microorganisms – i.e. sterile – is something that can be claimed only with a certain degree of probability.

European standard (EN) 556 based its definition of sterile medical devices on that of the European Pharmacopoeia: “An item can be viewed as sterile if the theoretical value of not finding more than one living microorganism in $1x10^6$ (1 million) sterilized units on the end product is assured.”

Accordingly, the aim of sterilization is to achieve a **S**terility **A**ssurance **L**evel (SAL) of 10^{-6}

Sterilization is one step of the procedure used to process or reprocess medical devices. The other steps of reprocessing are cleaning and disinfection. These “decontamination” measures are aimed at reducing the microbial count to such an extent that before sterilization the microbial load of heat-resistant microorganisms (with a $D_{121°C}$ value of 2.5 min, see below) present on the supplies can be assumed to be $\pm$ zero. To achieve a SAL of 10^{-6}, the sterilization process must be able to reduce the microbial count of heat-resistant microorganisms by 6 orders of magnitude (6 log levels). (see also Fig. 3).

2.1 Characteristic parameters for calculating the effectiveness of a thermal sterilization process (background information)

The effectiveness of a sterilization process can be calculated and evaluated on the basis of certain parameters that have been experimentally identified.

For an identified sterilization time T the associated holding time Z(T) can be calculated as follows:

$$Z(T) = n * D(T)$$

with $\mathbf{D(T) = 10^{(121\,°C - T) / z} * D\,(121\,°C).}$

Where:
n (desired microbial reduction) = 6,
$D_{(121\,°C)}$ = 2.5 min and
z = 8 K (for the temperature range to 128 °C).

The characteristic variables used here are primarily the microbial- and process-specific D values and z values.

2.1.1 D value

D value: the D value (decimal reduction time) is the time in minutes that is needed to reduce a population of a particular microorganism by one log level at a given temperature, corresponding to an inactivation rate of 90%.

The D value can be obtained from an experimentally identified survival curve or from an equation.

For example, spores of *Geobacillus stearothermophilus* at 121 °C have a D value of around 1.5 –2.5 min, and at 115 °C the D value is approx. 18 min.

2.1.2 z value

The z value gives the change in temperature in °C needed to cause a 10-fold change in the D value of an organism. z denotes the relationship between temperature and microbial inactivation and this is expressed in K (degree Kelvin as absolute temperature unit).

These values are based on calculation of sterilization parameters for processes using standardized sterilization parameters.

Microorganism (spore suspension in water)	D values in min at 115 °C ($D_{115°C}$)	D values in min at 121 °C ($D_{121°C}$)	z value (K)
Geobacillus stearothermophilus	15 - 24	1.5 - 4.0	6 - 7
Bacillus atrophaeus	2.2	0.4 - 0.7	8 - 13
Bacillus megaterium	0.025	0.04	7
Clostridium sporogenes	2.8 - 3.6	0.8 - 1.4	13

Tab. 1: D values and z values for some spore-forming bacteria (as per Wallhäußer, 1988)

Following the formula above the D-value for G. stearothermophilus at 134 °C is only a few seconds.

Other characteristic variables used for sterilization processes, such as the F value and degree of lethality, will not be discussed in detail here.

Lethality: The sterilizing effect, which is also called lethality or death rate, indicates the effect of a heat treatment, expressed as the number of decimal reductions in the number of microorganisms.

F-Value: The F-value for the process is the number of minutes required to kill a known population of microorganisms in a given item under specified conditions.

2.2 Spores

A number of groups of bacteria (spore-forming bacteria) are able to form highly resistant capsules (spores) when facing environmental conditions that are unfavourable to them. During sporulation, the cell plasma membrane largely “melts away” and the remaining spores can persist for years or even decades, while surviving unharmed external influences such as heat, cold, draught or exposure to disinfectants (see **Specialist Course Level I Script**).

These heat-resistant spores include bacteria that have major implications in surgery such as those causing gas gangrene (or gas oedema) *Clostridium perfringens, C. histolyticum, C. novyi* as well as the causative organism of tetanus *Clostridium tetani*. This is actually the reason why surgical instruments have to be sterilized, while thermal disinfection suffices for other bacteria, such as *Staphylococcus aureus,* which often cause postoperative wound infections.

2.3 Proof of sterility

Proof that a medical device is sterile cannot be provided by the end product. For a sterility test based e.g. on immersion (of the device) in a nutrient solution, in purely statistical terms more than one million of specimens would have to be investigated to demonstrate a SAL of 10^{-6}. Apart from the fact that a high level of secondary contamination would be likely, it would not be possible to detect all microorganisms or to use the devices after examination.

Therefore for many years now bioindicators have been used to verify the effectiveness of sterilization. This meant that germ carriers harbouring *G. stearothermophilus* spores of a defined resistance and population (microbial count) were exposed to the process and an investigation then conducted to see whether all spores had been killed.

In many facilities the use of bioindicators already has been replaced by physical tests for steam sterilization in the healthcare setting, with the entire pressure and temperature course of a cycle being recorded by means of thermocouples and pressure sensors. Based on the theoretical temperature it can be elucidated whether saturated steam conditions are assured at all sites within the sterile supplies. Verification of the test results by means of bioindicators, as was prescribed until recently (and continues to be stipulated in some cases by the authorities), can now be omitted in the case of sterilizers that are subjected to annual thermoelectric testing or of validated processes based on EN ISO 17665.

In many countries validation of sterilization processes is a legal requirement. Hence the sterilization process must be validated, i.e. to demonstrate that the requirements are being reproducibly met for each step of the process.

2.4 Killing behaviour

Please refer to Specialist Course Level I Script for information on the growth / reproduction of microorganisms.

The various types of processes that can be used for sterilization differ essentially in terms of their principle of action.

In steam sterilization microorganisms are quickly killed through denaturation (destruction) of their proteins. Conversely, superheated steam needs a longer time and a much higher temperature to effect killing, since under such conditions microorganisms are killed through oxidation processes. Sterilization in superheated steam is comparable with hot air sterilization (180 °C – 30 minutes). Superheated steam has a negative impact on the sterilization process since this steam does not, or does not adequately, condense and only steam that is able to condense will be able to transfer the requisite energy, in the form of the heat released during condensation, to the sterile supplies.

The sterilisation process must demonstrate evidence that the Sterility Assurance Level (SAL = the probability of a microorganism being present is equal to or less than $1:10^{-6}$) has been achieved for the respective sterilizer load. The specified sterilization conditions must be based on either

- a proven temperature/time relationship or
- experience of the bioburden (microbial load) on the respective medical devices and of the resistance profiles of such microorganisms.

In the healthcare setting only processes that meet the first condition are used.

Above the maximum temperature range at which microorganisms can survive, these are not, as one would expect, abruptly killed after a certain exposure time, rather a reduction in the microbial count takes place in accordance with an inactivation curve, which unfolds in the same way as a chemical reaction. As from the start of this exposure interval, the microorganisms are decimated in line with a logarithmic function. The following example is aimed at explaining how this proceeds in steam sterilization.

Saturated steam has a high heat content (energy) that is transferred through condensation to the cooler sterile supplies, thus killing any microorganisms present (see **Specialist Course Level I Script**). But since the energy released from the steam is not evenly distributed and, as such, condensation will not take place everywhere at the same time, all microorganisms cannot be killed at the same time.

The survival curve in Fig. 1 depicts this process on a graph.

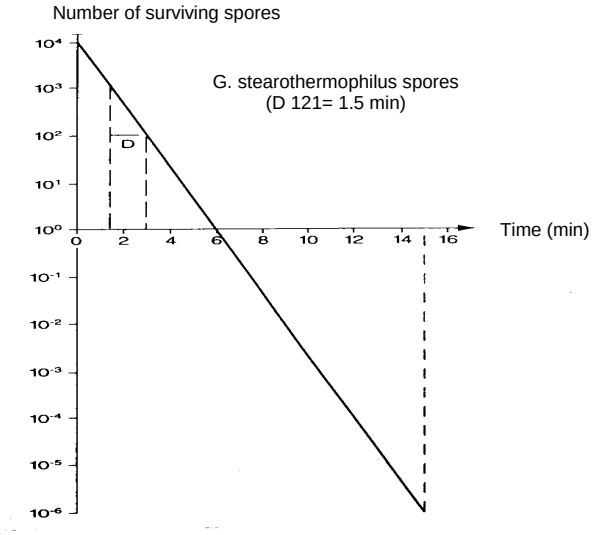

Fig. 1: Survival curve for *G. stearothermophilus* spores in saturated steam at 121 °C as a function of the baseline microbial count (as per Wallhäußer 1988)

From the above figure one can see that the time needed to kill the microorganisms present is dependent on the baseline microbial count. For a heat-resistant microorganism (e.g. *Clostridium perfringens*) with a $D_{121°C}$ value of 1.5 min and a baseline microbial count of 10,000, 15 min with saturated steam and a temperature of 121 °C are needed to achieve the requisite SAL of 10^{-6}. As outlined above, it is presently assumed that following decontamination the supplies to be sterilized are already to a large extent free of heat-resistant microorgansms, so that a baseline microbial count of $\pm$ 0 can be assumed. However, in reality a worst-case scenario based on a $D_{121°C-}$ value of 2.5 min is used here so that the curve movement will be confined to the negative range (see Fig. 2).

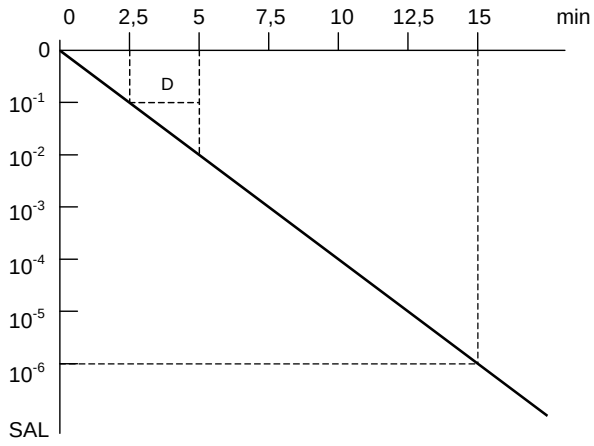

Fig. 2: Relationship between exposure time and SAL in steam sterilization (overkill process at 121 °C) for heat-resistant bacteria (spores of *G. stearothermophilus* with a $D_{121°C}$ value of 2.5 min)

3 Sterilization processes

3.1 General requirements for sterilization processes

The effectiveness of sterilization processes is determined e.g. by the following factors:

- Nature of the microorganisms present
- Baseline microbial count (Bioburden) and outcome aspired to
- Nature of medical device (the items to be sterilized)
- Process configuration
- Steam quality (or gas concentration)
- Temperature
- Holding time
- Sterile barrier system
- Loading pattern

Therefore to assure the safety of patients a number of general requirements must be met by sterilization processes.

- The sterilization process must be suitable for the supplies to be sterilized and should be as compatible with the respective materials.
- The sterilisation outcome must be reliable.
- Reprocessing and the requisite operating materials should as far as possible be environmentally friendly.

Hence the sterilizer, too, must meet certain essential requirements:

- It must be able to, at least, sterilize supplies without damage while enclosed in packaging suited to the process.
- Proof must be furnished that the decisive process parameters are complied with throughout the entire exposure time and in all parts of the supplies
- Proof must be furnished that after the exposure time the sterilant (sterilization agent) is removed from the sterilizer chamber and sterile supplies to such an extent that personnel will not face any hazards when unloading the supplies from the sterilizer.
- The sterilizer must be fitted with control instruments to indicate that the sterilant is present in the sterilizer chamber at an adequate concentration and that the temperature and other parameters of importance for the success of sterilization are complied with.

Specific requirements governing different sterilizers or sterilization processes are contained in national, European and international standards (see list of standards in annex).

3.2 Sterilization with moist heat

These processes use hot water, steam or steam-air mixtures. Temperatures of >115 °C are employed here.

For moist-air sterilization processes a distinction is made between processes that use steam as the sterilant (the steam must exert its action on the surface of the supplies being sterilized) and those where steam is used merely to transfer heat to hermetically sealed containers (ampoules, infusion bottles). In the latter case superheated steam, spraying of hot water or hot-air steam mixtures can also be used as a substitute for saturated steam.

3.2.1 Processes for sterilization of liquids (background)

For sterilization of liquids in sealed containers each container assumes somewhat the role of an autoclave since the liquid inside it is brought to the requisite temperatures, thus leading to a pressure build-up. Since in this case the equilibration times vary greatly as a function of the liquid quantities to be sterilized, the sterilization phase is triggered by a “product sensor”, which is placed inside the container and is representative of the greatest liquid quantity. Another point to be borne in mind is that cooling must unfold accordingly more slowly to prevent explosion of the container. In general a support pressure (i.e. artificially generated atmospheric pressure inside the chamber) is used.

3.2.1.1 Steam-air mixture process

This process operates in general with superimposed pressure, i.e. the pressure is not automatically generated by the steam pressure but rather is artificially maintained. Forced air circulation with ventilators is needed for uniform temperature distribution.

3.2.1.2 Direct hot-water spray process

This process is particularly suitable for sterilization of liquids where temperature precision is vital.(e.g. for temperature-sensitive plastic containers). A large volume flow of spray water must be supplied at a constant rate in a closed circuit during the various process steps.

3.2.1.3 Gravity displacement and Continuous flow processes (background)

In a gravity displacement as well as in a flow process the air is displaced by saturated steam and thus expelled from the sterilizer chamber and sterile supplies. Today, these processes are used only in laboratory autoclaves and steam sterilization systems employed to sterilize liquids in sealed glass bottles (however, this process continues to be used on a large scale in particular in medical practitioners' offices / doctors' surgeries). For sterilization of medical devices the air must be actively removed from the packaging, from hollow instruments and from porous materials (vacuum process).

3.2.2 Steam sterilization processes for reusable medical devices

Steam under pressure is understood to mean steam at pressure levels above the atmospheric air pressure (pressure > 1 bar relative). This pressure is automatically generated as soon as water is heated to above 100 °C and the steam is unable to escape; the pressure is, so to speak, a "by-product" of sterilization and is thus not a requirement.

3.2.2.1 Processes based on determination of the bioburden (background)

These processes are based on cognisance of the microbial load (bioburden) on the medical devices to be sterilized (determination as per EN 1174). Another point to be borne in mind when defining the process parameters is the microbial resistance to moist heat. Armed with this data, the requisite sterilization parameters can be elucidated. Since in the healthcare setting virtually only processes with standardized sterilization parameters (see below) are used, this topic will not be further elaborated on here.

3.2.2.2 Processes with standardized sterilization parameters

For steam sterilization the supplies to be sterilized are placed in pressure sterilizer chambers within which after air removal they are brought to the required temperature through exposure to saturated steam under pressure for a certain period of time. For sterile supplies that have been properly reprocessed the temperature/time combinations listed below are deemed sufficiently effective to achieve the prescribed Sterility Assurance Level:

- 121°C with a holding time of at least 15 minutes
- 134°C with a holding time of at least 3 minutes

The requirements are deemed to have been met if

- the temperature is within the sterilization temperature range (sterilization temperature as lower limit + 3°C)
- the difference between the lowest and highest temperature, including the theoretical saturated steam temperature, is not more than 2 K (°C)
- the temperature measured during the holding time does not fluctuate by more than 1K (°C)
- an equilibration time of 15 seconds for a chamber volume < 800 l or 30 seconds for a chamber volume > 800 l is not exceeded.

3.2.2.2.1 Vacuum process

- To shorten the heating time and equilibration time an obvious thing to do is to remove the air from the sterilizer chamber by generating a vacuum before introducing the steam.

The fractionated (pulsed) vacuum process is deemed to represent the state of the art for the steam sterilizers used for medical devices. In a fractionated vacuum process steam is admitted into the sterilizer chamber after evacuation and immediately afterwards the steam-residual-air mixture is removed again. This process (pulses) is repeated on several occasions. The better the vacuum generated and the greater the pressure difference achieved, the more successfully can removal of the residual air be carried out.

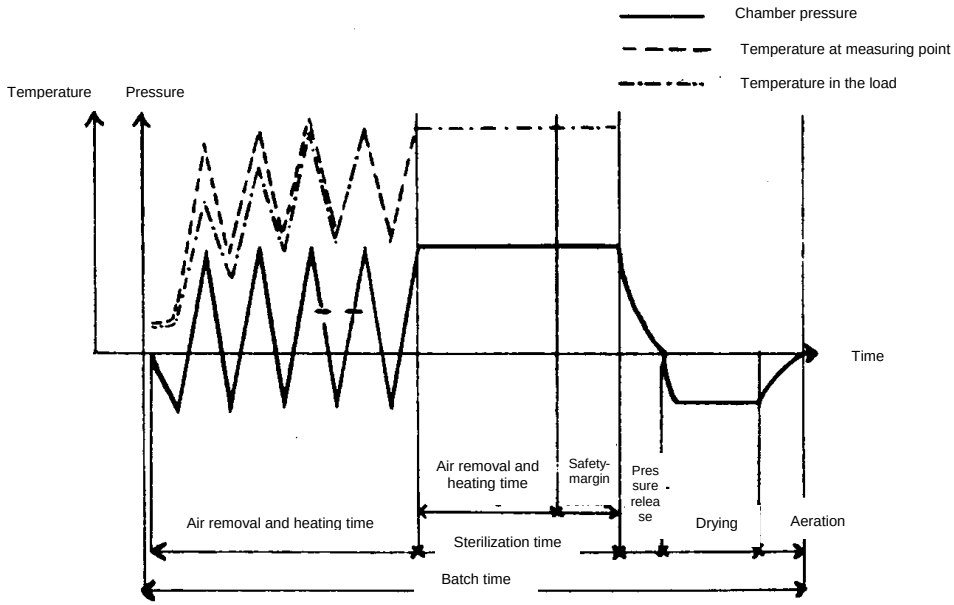

Fig. 3: Diagram showing the sterilization process using the fractionated vacuum method (as per G. Kraus, Vienna)

3.2.3 Steam sterilization of medical devices

Sterilization with saturated steam under pressure is currently deemed to be the most reliable method available for sterilization of reusable medical devices and is viewed as representing the state of the art.

3.2.3.1 Steam types, steam quality, temperature-pressure relationship

Since steam is used as the effective sterilant in steam sterilization and, as such, must come directly into contact with the sterile supplies, the properties of the steam play a pivotal role in determining the effectiveness of the sterilization process.

3.2.3.1.1 Saturated steam

If one introduces water into a sealed container and then removes the air, an equilibrium will be created between the liquid water and the steam. The pressure prevailing within the container will correspond exactly to the steam pressure of the water at the existing temperature. The term “saturated steam” is used to denote the nature of the steam present under such conditions ***(see also Specialist Training Course Level 1 Script)*.**

If one increases the temperature, water will continue to evaporate and thus raise the pressure until equilibrium is reached again. The steam in the container continues to be saturated.

It is present in dynamic equilibrium between evaporation and condensation. Hence there is a fixed correlation between the pressure of the steam and the temperature:

Pressure (mbar absolute)	Temperature (°C)
1208	105
1431	110
2048	121
3043	134
3937	143

Tab.2: Correlation between steam pressure and temperature

If one depicts the pressure as a function of the temperature in a diagram, one obtains the steam pressure curve of water (Fig. 4).

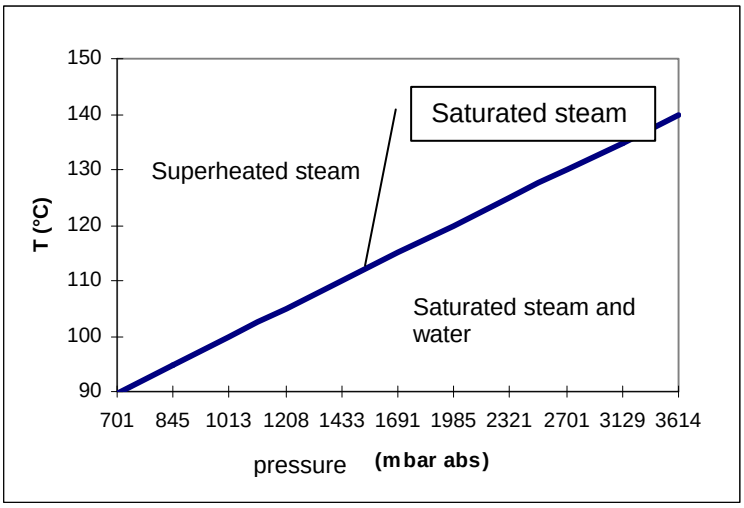

Fig. 4: Temperature/ pressure relationship for saturated steam (saturated steam curve, schematical)

If the pressure of the steam at a particular temperature is on this curve, then the steam will be saturated (hence the term “saturated steam curve”).

As already mentioned the protein of bacterial cells is denaturated (destroyed) by the energy released through condensation of saturated steam, and the bacteria thus killed.

Hence sterilization with steam is dependent on the presence of saturated steam.

If the sealed container is further heated, the entire water will have evaporated at some point. If more energy is supplied to the steam, superheated steam will be generated.

3.2.3.1.2 Superheated steam

A characteristic of this is the absence of a relationship between the pressure and temperature. Based on the pressure measured, the steam should have a lower temperature value.

If superheated steam comes into contact with a colder medium (supplies) it will release part of its energy, thus heating up the supplies but the steam itself persists in its original form.

But since it is condensation on the sterile supplies (and the energy thus released) that is responsible for the microbicidal action of a steam sterilization process, only saturated steam is suitable for steam sterilization. The temperatures alone would not be enough for sterilization (see hot air sterilization).

What can cause superheated steam?

- **The jacket temperature is higher than the chamber temperature**: the jacket temperature should be 1 – 1.5°C higher than the sterilization temperature. If the temperature is too low, it will “rain” within the sterilizer and overheating will result from too high a temperature.
- **Pressure reduction line leading to the chamber too short:** the lead (line) between the last pressure reduction mechanism and the connection to the steam sterilizer should be at least 4 m. If this pressure reduction line is situated closer to the sterilizer, it can give rise to noticeable overheating of the steam.
- **Exothermal reduction:** hygroscopic (= attracting moisture) materials such as cellulose, cotton, etc. have a tendency to cause overheating at the time of steam condensation (water absorption process) due to rehydration, if they are too dry prior to sterilization (this has been noted for relative humidity < 35 %) or if they undergo dehydration (i.e. become dried out) during the process. This means that such a danger exists, in particular, if the laundry is very dry (e.g. mangled or ironed) or following operating mistakes. (Example: the sterilizer is loaded with textiles and the door closed but the programme is not started because one container is still missing; the textiles will become very dry because of the heat radiated from the jacket). For this reason hygroscopic materials have to be conditioned prior to sterilization.

  Exothermal reactions may also be due to lack of, or unsuitable, jacket control: because of the heat radiated from the jacket to the sterile supplies (around 139 °C at 2.5 bar relative pressure) cellulose materials can become ultra dried out during the fractionation phase (evaporation point at 100 mbar abs. approx 46 °C).

3.2.3.1.3 "Wet steam" or "supersaturated steam":

Unlike superheated steam, where the temperature is higher than the pressure, in supersaturated steam the temperature and pressure are equal. Strictly speaking, the term "wet steam" is misleading because steam that is saturated (i.e. saturated steam) will not be able to absorb any more water than it already contains; such a situation gives rise to excessive condensation, thus producing saturated steam and water. One characteristic of wet steam is that it condenses spontaneously (i.e. without having to come into contact with surfaces).

While wet steam is endowed with microbicidal action, wet packaging is less able to protect against penetration of microorganisms and hence the sterile supplies will not lend themselves to storage.

Causes:

- **Condensate entrained with steam:** pressure reduction valve located too far from chamber
- **Steam generator too small:** boils over constantly, hence there will also be water in the steam
- **The jacket pressure is lower than the chamber pressure:** jacket will thus be cooler, the steam condenses and it will "rain" when steam is admitted to the chamber.
- **Unsuitable configuration of steam lines (pipes)**

Note:

Drying problems occur not just because of "wet steam" but also due to the following factors:

- Loading mistakes: instruments positioned too close to each other
- Instrument piles or separate instruments too heavy
- Excessive condensation during fractionation phase (e.g. steam admitted too quickly to chamber)
- Instruments piled on cold surfaces immediately after sterilization

Accordingly, prolongation of the drying phase will not always solve this problem. Furthermore, if evacuation is too rapid during drying the supplies will cool down too quickly thus giving rise to condensation. It may be possible to overcome this problem by using "fractionated drying" (i.e. the supplies are heated up by subsequently supplying steam and will thus dry more quickly).

3.2.3.1.4 Feed water

Since steam exerts a direct action on the sterile supplies, the feed water (water for steam generation) must be free of impurities that could adversely affect the sterilization results or cause damage to the sterilizer or sterile supplies.

Tab. 2 lists the guide values given in EN 285 for impurities in feedwater and condensate.

	Feed water	**Condensate**
Conductivity (at 25°C)	≤ 5 µS/cm	≤ 3 µS/cm
pH value	5 to 7.5	5 to 7
Colour	colourless, clear, no residues	colourless, clear, no residues
Hardness	≤ 0.02 mmol/l	≤ 0.02 mmol/l
Evaporation residues	≤ 10 mg/l	-
Silicates (Si O_2)	≤ 1 mg/l	≤ 0.1 mg/l
Iron	≤ 0.2 mg/l	≤ 0.1 mg/l
Cadmium	≤ 0.005 mg/l	≤ 0.005 mg/l
Lead	≤ 0.05 mg/l	≤ 0.05 mg/l
Heavy metals apart from iron, cadmium, lead	≤ 0.1 mg/l	≤ 0.1 mg/l
Chlorides	≤ 2 mg/l	≤ 0.1 mg/l
Phosphates	≤ 0.5 mg/l	≤ 0.1 mg/l
Note: the use of feed water or steam with constituents higher than the values given in Table B1 can greatly shorten the sterilizer service life and invalidate the manufacturer's warranty or guarantee.		

Tab. 2: Permissible levels of impurities in condensate and feed water (from EN 285, Table B1 and B2)

The quality of the feed water must be monitored (preferably daily measurement of conductivity) and documented.

To achieve a sterilization effect the steam must be able to reach the microorganisms present on the surfaces of medical devices, i.e. the items shall be clean and the steam must as far as possible be free of non-condensable gases (air, CO_2, "inert gases").

Steam is a condensable gas (present in liquid form at normal ambient pressure). Air (or CO_2, nitrogen, oxygen, carbonic acid gas) is a non-condensable gas (mixture) (non-condensable gas is present as a gas at normal ambient pressure). If steam contains too large amounts of non-condensable gases (NCGs), these can build up in hollow bodies and porous materials.

The proportion of non-condensable gases should not exceed 3.5 % (volume percent).

3.2.3.2 Sterilizer types

Steam sterilizers come in different sizes and are designed for the most diverse applications.

In principle a distinction is made between load (or batch) sterilization and continuous sterilization processes.

Steam sterilizers for continuous operation are used predominantly in the foodstuffs industry and for sterilization of infusion solutions in the pharmaceutical industry. Their operation is generally based on a 3-phase system: Prewarming-Sterilization-Cooling, with the various steps unfolding in different interconnected chambers.

In the healthcare setting only **batch sterilizers** are used.

Based on the sterilizer size, one distinguishes between:

- small steam sterilizers and
- large steam sterilizers

3.2.3.2.1 Small steam sterilizers

are sterilizers whose capacity is less than one sterilization unit.

The small steam sterilizers currently in use generally are operating with internal steam generators and operate according to the continuous flow process. They are used, mainly as tabletop models, in medical and dental practices as well as in laboratories. Many of these sterilizers are not equipped with the safety mechanisms required pursuant to the latest European standards and often are operated manually, thus making it impossible to provide evidence of a reproducible sterilization process. Nor is there any recording facility (batch printer, recording unit) generally available. These types of old sterilizers should not be used any more.

One version of the small steam sterilizers is the “flash sterilizer” commonly used in decentralized sterilization units or in operating theatres to assure rapid reuse of contaminated surgical instruments. These types of sterilizers should not be used any more.

Pursuant to EN 13060 (2004), a distinction is made between three different types of sterilization cycles for small steam sterilizers depending on their intended use. This distinction derives mainly from the nature and method of air removal. The greater the degree of air removal, the easier it will be to prevent formation of residual air pockets within which complete inactivation of microorganisms is not assured.

- **Type N sterilization cycles** (“**n**on wrapped”) operate as per the flow or gravitation method, i.e. the air present in the chamber and supplies is not actively removed but rather is displaced and expelled from the chamber by the incoming steam. This cycle may only be used for non-wrapped, solid medical devices.

Note: (e.g. as a substitute for thermal disinfection in a WD for certain dental instruments). In this case one should be aware that the medical devices are not to be labelled as sterile and stored as such.

Type N sterilization cycles are not suitable for sterilization of medical devices because they must be packed before sterilization. Therefore when investing in new sterilizers one should purchase those able to execute types B cycles and which demonstrably meet the requirements of EN 13060 (declaration of conformity required!).

- **Type S sterilization cycles** ("**s**pecified") generally operate according to the pre-vacuum method. The chamber is evacuated only once to remove the air from it. These cycles are suitable for sterilization of items specifically designated as such by the sterilizer manufacturer (e.g. for hand and angled pieces in dentistry).
- **Type B sterilization cycles** ("**b**ig") operated in accordance with the fractionated vacuum method where the air is actively expelled by means of repeated evacuation followed by admission of steam. These can be used to sterilize virtually all medical devices, e.g. wrapped, solid, hollow and even porous sterile supplies.

3.2.3.2.2 Large steam sterilizers

Large steam sterilizers are sterilizers with a capacity greater than or equal to one sterilization unit.

In general steam generation in large steam sterilizers is based on inbuilt electric steam generators (sterilizers with internal steam generator) or on connection to a main steam generation facility within the establishment (sterilizers with external steam generator).

3.2.3.3 Functional sequence

The functional sequence of steam sterilization essentially entails three steps.

Air removal phase

To remove as far as possible all air from the sterilizer chamber and the sterile supplies, the chamber is evacuated repeatedly followed by introduction of steam (= fractionated vacuum process). If there are any remaining air pockets (e.g. in porous materials), successful sterilization cannot be guaranteed.

Conversely, the temperature inside the sterile supplies lags behind that prevailing in the chamber. The period which elapses between the attainments of the sterilization temperature in the chamber and the attainment of this temperature in all parts of the supplies to be sterilized is called the **equilibration time** (in fractionated vacuum processes this is generally in the range of a few seconds, see above)

Sterilization phase

This consists of the holding time + equilibration time (= plateau time).

For the standard process (121 °C) the holding time is 15 min, and 3 min at 134 °C (EN 285).

Note: *In practice safety margins are added to the above (e.g. 121 °C/20 min, 134 °C/ 5 min).*

Drying phase

Drying following sterilization also constitutes an important process step. Again, drying is effected through evacuation of the chamber (since the boiling point of water is lower at negative pressure, the condensate produced will evaporate more quickly), while the sterile supplies are cooled down at the same time, followed by pressure equilibration.

The moisture content of the sterile supplies following sterilization must not exceed certain tolerance limits (see above).

European standard EN 285 regulating large steam sterilizers specifies, in addition to technical requirements for pressurized containers, steam generators, air filters, vacuum systems, instrumentation, indicator devices, etc., also test methods and **performance requirements** for the process:

Physical values

Sterilization temperature range:

- The sterilization temperature range must contain the lower limit value specified by the sterilization temperature and an upper range value +3 °C.

Small load (standard test pack):

- The equilibration time must not exceed 15 s for sterilizer chambers up to 800 l or 30 s for bigger sterilizer chambers
- The temperature measured during the plateau time above the test pack must not exceed the chamber temperature by more than 5 °C during the first 60 s and by not more than 2 °C during the remaining time.
- During the holding time the temperature measured in the chamber and in the centre of the test pack must be:
    - within the sterilization range
    - not deviate by more than 2 °C from each other
- The holding time must not be less than 15 minor 3 min for the corresponding sterilization temperatures 121 °C or 134 °C.

Full load:

- The chamber temperature measured at the end of the equilibration time and that in the geometric centre and beneath the uppermost towel in a standard test pack, arranged in a test load, must be within the sterilization temperature range.

Apart from this, the same values applicable to the small load must be complied with.

Air removal and steam penetration (Bowie & Dick test):

- The indicator placed in the middle of the standard test pack must show a uniform change in colour as per the manufacturer's instructions.

Leakage rate (vacuum test):

- The rise in pressure must not exceed 13 mbar for a measuring time of 10 min.

Dryness of the load:

Textile load:

- The mass of the test pack must not increase by more than 1%.

Metal load:

- The mass of the test load must not increase by more than 0.2%.

3.2.3.4 Minimum requirements for sterilizers commissioned before the release of EN 285

- Process control via absolute pressure measuring sockets
- Pressure and temperature recording for process control
- Separate temperature sensors for control and display
- Bowie & Dick test programme
- Vacuum test programme
- Adequate air removal
- Compliance with sterilization temperature range
- Correspondingly short equilibration times

3.2.3.5 Operation

Hygroscopic materials:

The relative humidity before sterilization is a limiting factor in the case of hygroscopic materials (i.e. those that "attract" water / moisture) such as cotton, paper and other cellulose items. Materials that are too dry give rise to an exothermal reaction, i.e. the material depletes the steam of its moisture when it comes into contact with it, thus giving rise to instances of local overheating (see saturated steam curve). This is generally observed for items with a relative humidity of less than 35 %, while overheating by up to 6 °C is something that often occurs. If such materials are sterilized (e.g. freshly mangled textiles) it is important to condition them (bring them into line with ambient conditions) before sterilization. For the same reason the relative ambient humidity on the clean side (of the sterilisation department / unit) should not be lower than 35 %. (see also "superheated steam")

Hollow bodies:

Until recently the helix model served to conjure up a worst-case scenario. But in the meantime we know that it is more difficult to remove air from hollow bodies with larger diameters (e.g 8-10 mm).

The chief determinant of this difficulty in removing air is the ratio of the volume to the internal surface. For example, a tube with a 4 mm diameter and 2 m length presents somewhat the same difficulty as a tube with a 2 mm diameter and 4 m length.

The depth of the 1st vacuum as well as the number of evacuation steps are decisive factors in air removal.

Double-ended open hollow bodies exhibit the same behaviour as single-ended open items of half the length, but in the latter case the air can accumulate only at the end of the tube.

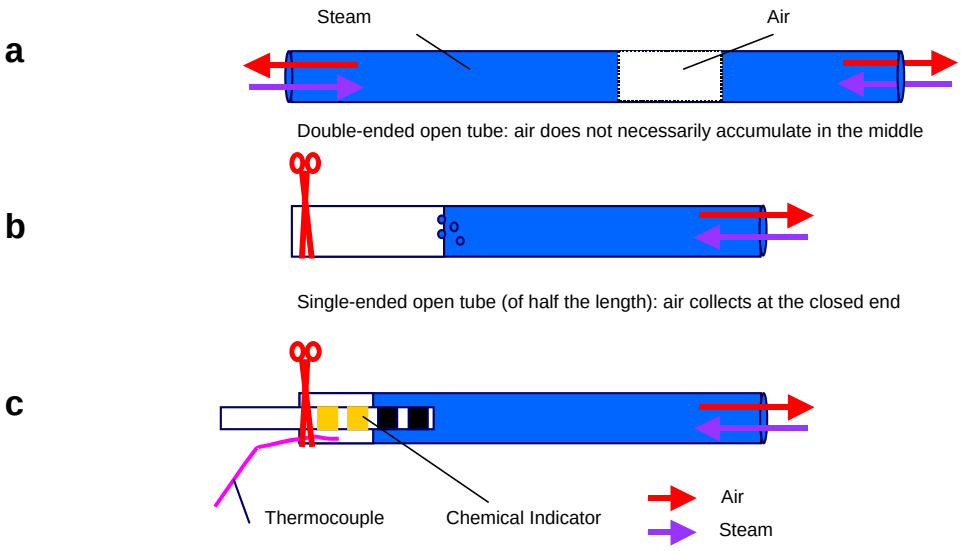

Fig. 5: Behaviour of air in hollow bodies

By means of a simple test it can be established whether the sterilizer is able to remove air from the hollow bodies (tubes) used and thus sterilize them. One takes a tube with the same dimensions as the longest tube used, but with only half the length. A chemical indicator is inserted at one end (e.g. from the helix model) and this end is closed with a strong clamp (see Fig. 5 c). Following sterilization one checks whether all indicator fields have undergone a change in colour. If that is not the case the tubes must be shortened accordingly.

3.2.3.6 Sterile barrier system (SBS)

The SBS should protect the sterile supplies against microbial recontamination while they are being withdrawn from the sterilizer chamber, during storage or transportation and up till the time of use. The SBS should be labelled showing their contents, type and date of sterilization as well as the batch number.

The SBS must not impede expulsion of the air from the supplies or penetration of steam into them. Items must be placed in their packaging such that no air pockets can be formed.

The protective function and subsequent drying of the packaged supplies must not be adversely affected by condensate.

The SBS used may be rigid reusable containers, paper, paper foil packaging etc. (soft packaging). The requirements to be met by the packaging as well as its suitability are

specified in the international standards EN ISO 11607-1 and -2 as well as in the European series of standards EN 868.

See Specialist Training Course Level I Script "Packaging"

3.2.3.7 Loading

In principle operation of sterilizers may only be entrusted to trained personnel who are conversant with the operating instructions (see chapter on Training).

The sterilizer chamber must be loaded as per the operating instructions of the respective sterilizer (no overloading of the chamber).

Arrangement of supplies within the sterilizer chamber

The sterilization containers or packages must be arranged in the sterilizer chamber such that steam penetration is not prevented, while facilitating air expulsion.

The shelves (false floors) in the loading trolleys should be perforated. The packs must not come into contact with the sterilizer chamber.

For mixed loads (e.g. instruments in containers and individually wrapped sterile supplies) the heavier items must be placed on the lowest level (condensate collection.

3.2.3.8 Programme selection

The programme selected will depend on the type of supplies to be sterilized, as specified in the operating instructions. For mixed loads make sure that the more temperature-sensitive items in the load are not damaged and that provision is made for adequate drying.

In general large steam sterilizers have 2-3 sterilizations programmes, a Bowie & Dick test programme, an automatic vacuum test and, if applicable, one or several additional programmes for special sterile supplies (e.g. prolonged drying phase for heavy items or a "prion programme").

e.g.:

P1: Vacuum test

P2 Bowie & Dick test

P3: Universal programme (instruments, textiles); 134 °C/ 5 min

P4: Synthetics (heat-sensitive material); 121 °C/ 20 min

P5: As P1, but with prolonged drying

P6: "Prion programme"; (as P1, but 134 °C/ 18 min)

3.2.3.9 Posttreatment (drying)

During sterilization water is formed on the sterile supplies (condensate); these must therefore be dried after sterilization in the sterilizer chamber (drying time). The sterilized items must be withdrawn from the chamber only in a dry state since moisture can adversely affect the protective function of the packaging. In any case any residual moisture present should dry out

after a maximum of 5 min. Condensate is also formed when hot sterile supplies are placed on cold surfaces, hence they should be allowed to cool down on the loading trolleys.

3.2.3.10 Validation, routine control and maintenance

With respect to validation and routine monitoring, European standard EN 554: “Sterilization of medical devices; validation and routine control of sterilization by moist heat” from 2006 has been replaced by the international standard EN ISO 17665-1; Part 2, “Guidance on the application of Part 1”, to a large extent explains the standard requirements in greater detail. However, essentially no changes have been made to the main validation procedures.

See module “Validation” and “Quality Management”

3.2.3.10.1 Preproduction tests

Before placing the sterilizer in operation each day a steam penetration test (Bowie & Dick test - BD test) must be conducted.

Once the Bowie & Dick test programme has been completed, the indicator must show a uniform change in colour (as per the manufacturer’s instructions). Otherwise, steam penetration is not guaranteed. If the sterilizer has not been in operation for a long period of time air may have accumulated in the steam lines and have given rise to a “failure” result in the BD test. In such cases a “pass” result is obtained on repeating the test. If one is already aware of such a situation it is recommended that a blank load (using the “heating programme”, which is the shortest programme available) be run before the BD test.

Alternative BD-Test Systems might be used if the compliance with the criteria given in EN ISO 11140-4 is proved.

Furthermore, a vacuum test (VT) must be conducted at specified intervals (at least weekly). Some sterilizers have a heating programme integrated into the vacuum test. The rise in pressure during the test time (10 min) must not exceed 13 mbar.

If the pressure increase exceeds 10 mbar/10 min the VT should be run daily.

3.2.3.10.2 Batch control

A recorder (digital or analog printout of measured values; printer or recording device) must continuously record all process-relevant pressure and temperature data to document compliance with the sterilization conditions. This printout/log is the most important criterion for release of the sterilization batch.

A reprocessing indicator (adhesive label) must be affixed to each sterilization container or packaging so that one can immediately recognize whether its contents have already been subjected to a sterilization process or not.

Batch control systems (e.g.in the form of a helix) containing chemical indicators (PCD= process challenge device) can be used additionally. This PCD is intended to simulate a worst-case scenario and can be useful when releasing sterile supplies. The results of these tests have to be recorded, the indicators themselves need not to be kept, because the colour of the indicators might change by time.

See also module "Quality Management"

3.2.3.10.3 Maintenance

Maintenance tasks must be conducted as per the manufacturer's instructions and then documented. A maintenance schedule must be compiled, i.e. all tasks to be discharged should be listed together with their relevant intervals. (This applies for all equipment in the Reprocessing Unit for Medical Devices (RUMED), i.e. also for washer-disinfectors, ultrasonic equipment, heat sealing machines, etc.)

An equipment log book must be maintained, listing all maintenance/ servicing tasks, repairs and tests.

To remove any impurities that will have accumulated in the steam generator, it must be desludged at least once daily by opening the empty valve (a better approach would be automated desludging around every 30 min).

3.2.3.11 Safety regulations

Sterilizers must of course meet a number of safety requirements (electric, mechanical, electromagnetic compatibility with other equipment, etc.) to rule out potential hazards to operating personnel. These are set out in EN 285.

3.3 Low-temperature sterilization processes

Gas sterilisation processes are based on the microbicidal action of gases (chemical sterilization processes). Since this microbicidal action can be unleashed only if the gases come into direct contact with the microorganisms, the suitability of the sterilization gas used will depend on its ability to penetrate into the sterile supplies and on the surface composition of the sterile supplies.

The sterilization gases used in practice are ethylene oxide (EO), vaporized formaldehyde (FO) and hydrogen peroxide gas.

Because of the high toxicity of sterilization gases, gas sterilization processes should only be used in settings where, because of their characteristics, the sterile supplies will not tolerate steam sterilization processes (heat-sensitive items).

3.3.1 Sterilization with ethylene oxide

For gas sterilisation with ethylene oxide the items to be sterilized are exposed to EO in a gastight, sealed chamber. The high penetration capacity of EO is an important property in assuring a good, and relatively fast, sterilizing effect. Gas concentrations of around 450-1000 mg per litre of empty sterilizer chamber volume are used for sterilization.

Ethylene oxide gas sterilization is regulated by EN 1422 (ethylene oxide sterilizers – requirements and test method). ISO 11135 regulates validation of ethylene oxide sterilization processes, while the safety regulations in some countries are governed by Technical Regulations on Hazardous Substances.

3.3.1.1 Properties of ethylene oxide

Under atmospheric conditions ethylene oxide is present as a colourless gas with a slightly ethereal odour, but with an average odour threshold of 700 ml/m^3 it does not have any definite sensory warning properties. Extreme caution is needed when using EO since it can form explosive gas mixtures when it comes into contact with air. The ignition point is 40 °C. Pure EO too disintegrates in an explosive manner when heated.

Other disadvantages of EO are its high toxicity and carcinogenic effect:

- EO is a potent protoplasmic toxin. It can be taken up by the body orally, by inhalation or via the skin. At the high concentrations used for sterilization it can be lethal to humans.
- EO is carcinogenic (= causes cancer) (assigned to Category C2). Clustering of cases of leukaemia and stomach cancer has been reported in exposed persons.
- Based on its mutagenic (=genotoxic) effect, EO has been assigned to Category M2. Genetic studies have revealed that damage to DNA rises significantly in tandem with increases in ethylene oxide concentration in the room and alveolar air.
- The allergizing properties of ethylene oxide poses a risk to not only the staff entrusted with EO sterilization but also to healthcare workers in general and to patients. The allergic effects observed relate to the skin and mucosa. Allergic reactions, including even anaphylactic shock, can occur in patients (primarily those on dialysis).
- The chemical-irritant effect manifests on the skin and mucosa of the respiratory tract following irritation of varying degrees of severity.
- Systemic effects on the central nervous system (headache, nausea, vomiting, anxiety, or even loss of consciousness), heart and other organs have been described as acute forms of intoxication. Chronic intoxication gives rise to damage to the central and peripheral nervous systems as well as to the liver, kidneys and testicles.

3.3.1.2 Limit values for EO

The NIOSH (National Institute for Occupational Safety and Health) recommended exposure limit (REL) for EO is 0.1 ppm as an 8-hour time weighted average (TWA) with a 10 min ceiling limit of 5 ppm.

NIOSH has determined that 800 ppm is the EO-concentration that is immediately dangerous to life and health.

3.3.1.3 Absorption and Desorption

Following ethylene oxide sterilization the sterile supplies are not ready for immediate use since the poisonous gas will have adsorbed (bound to) on them. Therefore the valid desorption (degassing) time periods must be observed. (For deaeration in heated deaeration chambers with repeated air exchange this is 18-24 hours for most items).

During sterilization EO penetrates into the sterile supplies and adsorbs (becomes deposited) on their surfaces. On completion of sterilization, the amount of gas absorbed will be released again more or less fast as a function of the composition of the supplies. This process is known as desorption. The desorption time pursuant to DIN58948 is the period of time needed after gas sterilization to remove the sterilisation gas from the sterile supplies to such an extent that they can be used for the intended purpose. To avoid damage to health when using the sterile supplies, the regulation compiled by the former German Health Office (BGA Berlin in 1986) states that no ethylene oxide residues should be detectable on the sterilized supplies – including any packaging – after the desorption time using validated methods with a detection sensitivity of at least 1 ppm. For the likewise toxic halogenated ethylene hydrin (breakdown product of ethylene oxide) a limit value of 150 ppm has been specified. Desorption of EO and its by-products will depend on the following factors:

- Amount of ethylene oxide absorbed
- Sterilization time
- Type and thickness of the supplies (softeners)
- Packaging material and method
- Temperature during deaeration
- Type of aeration method (number of air exchange cycles)

The deaeration times needed cannot be predicted as a general rule because of these different variables of influence. Since only those items for which the manufacturer has confirmed that they cannot be made from other materials compatible with other sterilization processes may be sterilized with EO, and it is after all the manufacturer who is most familiar with his materials, the sterilization and desorption conditions should be specified by the manufacturer (see EN 30993-7: Biological testing of medical devices; EO sterilization residues).

In practical terms, desorption takes place in deaeration chambers with air extraction or in special degassing cabinets. Desorption can be expedited through high temperatures.

3.3.1.4 Method of action and functional sequence

The microbicidal activity of EO and hence the sterilization results achieved are a function of various parameters:

- **Ethylene oxide concentration**: doubling the EO concentration reduces the sterilization time needed by half.
- **Temperature**: raising the temperature from e.g. 20 °C to 50 °C the inactivation time is reduced to 1/6. The spectrum of action is approx. 55 °C.

- **Humidity**: EN 1422 recommends a relative humidity of 40-85% for sterilization with ethylene oxide. In numerous cases this is a limiting factor because the requisite humidity cannot be assured for every item. This humidity needed in the item to be sterilized can be generated either outside the sterilizer chamber in an air-conditioned room (preconditioning) or effected as part of the sterilization process within the sterilizer chamber (humidification).
- **Pressure**: the pressure used for EO sterilization also plays a pivotal role. For example raising the pressure from 1 bar to 7 bar shortens the microbial inactivation time by 40-85% (depending on the ethylene oxide concentration).
- **Exposure time**: since the exposure time needed is a function of all the variables already mentioned, it is scarcely possible to calculate it. In most cases this exposure time is determined on the basis of experiments conducted with bioindicators.
- **Packaging**: the packaging must be permeable to both steam and EO. The use of transparent sterilization packaging is recommended, while avoiding the use of packaging made entirely of foil.

3.3.1.5 Operation

- **Preparation of the sterile supplies:** before sterilization the supplies to be sterilized must be thoroughly disinfected and cleaned. After cleaning, rinse thoroughly with distilled water or demineralised water, paying special attention to any hollow cavities (making sure there are no microorganisms embedded in salt crystals). Then the items to be sterilized must be carefully dried, again ensuring that there are no liquid residues in hollow cavities.
- **Placing the sterilizer in operation:** the sterilizer may be placed in operation only by trained personnel, while observing the manufacturer's instructions.
- **SBS**: the **SBS** must be permeable to both steam and EO (see above).
- **Loading**: the supplies to be sterilized should in principle be placed in sterilization trays or in other suitable containers. The supplies used for a load should not occupy more than 75% of the sterilizer chamber volume and must not come into contact with the chamber walls. These items should be packed loosely to assure adequate air circulation.
- **Deaeration**: following sterilization the deaeration should take place in the sterilization chamber itself. Otherwise the sterile supplies must be stored in appropriate deaeration or degassing chambers.
- The desorption times must be specified by the manufacturer (see above). Empty gas cartridges should be degassed as well.
- **Storing the sterilization gas**: a dedicated closed room, which is properly supervised and ventilated, must be available for storage of sterilization gas cartridges or pressure canisters.

3.3.1.6 Testing, validation and routine control

EN 550 sets out the procedure used for validation of EO sterilizers. The load used here is based on operating instructions. **Microbiological testing** is done with bioindicators. The number of bioindicators needed will depend on the size of the sterilizer chamber, composition of the sterile supplies and type of packaging. For sterilizers with a usable volume <150 l at least 10 bioindicators are used, and at least 20 for bigger usable volumes.

The test organism used is *Bacillus atrophaeus*. ISO 18472 gives information on manufacture, testing and use of bioindicators.

The pressure course within the sterilizer chamber is monitored with a recorder. Thermoelectric control is not mandatorily specified.

Periodic microbiological testing of the sterilizer should be conducted every six months or after each 200 sterilization batches.

Validation consists of commissioning as well as of physical and microbiological performance qualification.

Routine control consists of monitoring and recording of process-relevant parameters: pressure, temperature, time, (humidity, gas concentration). Since the last two parameters are incorporated only into (expensive) industrial sterilizers, it is virtually impossible to conduct parametric release for the sterilizers used in the healthcare setting. This is another problem when using EO processes in the healthcare sector.

An adhesive label should be affixed to each sterilization container or an indicator should be featured on the packaging. While visual inspection (change in colour of chemical indicator) is necessary it is no reason to assume that the supplies are sterile. It merely helps to differentiate between items that have undergone a sterilization process and those that have not.

See Module "Validation"

3.3.1.7 Maintenance / servicing

Maintenance or servicing tasks must be performed regularly on the sterilizer in accordance with the manufacturer's instructions given in the operating manual. Major maintenance and repair tasks must be conducted by the manufacturer.

3.3.1.8 Safety regulations

EO must only be used in fully automated sterilizers. Sterilization must be carried out by persons who have the necessary expertise (certification of qualification). A sterilization manager, with commensurate qualifications, must be appointed to take charge of sterilization. The sterilization manager must be present for all important process steps, e.g. replacement of

pressure gas canister, leakage tests, programme start, supervision of degassing and withdrawal of sterile supplies from the sterilizer, disposal of the sterilisation gas containers. The sterilizer must not be installed in an area normally used for other working activities. In the case of two-door sterilizers, this only applies for the unloading side. The room where the ethylene oxide sterilizer is installed must be adequately ventilated (12-fold air exchange per hour). Compliance with the technical guide concentration values in the workplace must be monitored. Ethylene oxide sterilization must not be entrusted to adolescents younger than 18 years or to pregnant women. The permanent monitoring of the EO concentration in the surrounding of the sterilizer should be performed.

Staff operating ethylene oxide sterilizers should be specially trained.

Elimination of EO: the Technical Guide to Maintenance of Air Purity specifies a threshold value of 25 g/h for elimination of ethylene oxide. Since in EO sterilizers 80-90% of the ethylene oxide used is extracted in the first few minutes after sterilization and the threshold value is thus exceeded, provision must be made for installation of an ethylene oxide elimination unit connected after the sterilizer (temporary exemptions have been granted to older sterilizer modules). Elimination is effected through chemical flushing (conversion to ethylene glycol when using sulphuric acid as a catalyser), burning off (with propane gas as carrier gas in bigger systems) or by means of a catalyser (precisely dosed EO-air mixture is transported by means of a heated precious metal fill and disintegrates to carbon dioxide and water).

3.3.2 Sterilization with steam formaldehyde

Sterilization with low-temperature steam-formaldehyde (LTSF) processes is an alternative to ethylene oxide processes. Its advantages compared with EO processes reside in the fact that the formaldehyde-steam mixture used is neither flammable nor explosive and that after the sterilization cycle it can be removed from the sterile supplies to such an extent that there is no need for deaeration and sterile supplies are thus immediately available for reuse.

Its drawback is that – compared with ethylene oxide – it is less well able to penetrate into the sterile supplies.

In formaldehyde processes formaldehyde and steam are combined at temperatures of 55 °C to 75 °C for microbicidal action. Neither steam alone nor dry formaldehyde gas are able under these conditions to kill spores. Only the combination of both substances generate the level of microbicidal activity needed for sterilization.

Since the water and formaldehyde pressure prevailing under the operating temperatures used is always below the atmospheric pressure, formaldehyde sterilization is carried out in principle at sub-atmospheric (negative) pressure.

Air is removed from the sterilizer chamber and sterile supplies by means of a fractionated vacuum process. Once the requisite sterilization time has elapsed, formaldehyde is removed from the sterile supplies through steam pulses with fractionated evacuation. This is followed by purging with air.

3.3.2.1 Properties of formaldehyde

Formaldehyde is used for sterilization in the form of an aqueous solution with a formaldehyde concentration of 2-5%, also commercially available in this form. It has a pungent odour, with an odour threshold of 0.05-1.0 ppm. Concentrations of 2-3 ppm formaldehyde in the respiratory air cause a stinging and burning sensation in the noose, eye and throat, attesting to the fact that formaldehyde, unlike EO, is endowed with excellent warning properties.

Spending time in environments with formaldehyde concentrations over 30 ppm can cause severe damage and even death. As well the carcinogenic potential of FO is proved.

FO has also been classified as a substance that presents a special risk of absorption through the skin as well as a risk of skin sensitization.

The NIOSH recommended exposure limit (REL) 0.016 ppm [0.02 mg of FO/ m^3 of air] as an 8-hour TWA and 0.1 ppm (0.15 mg /m^3) as a ceiling concentration determined in any 15 min sampling period.

3.3.2.2 Absorption and desorption of formaldehyde

Since formaldehyde has a lower penetration capacity than EO, it is less well absorbed by the sterile supplies. Thanks to the intensive measures conducted following the sterilization process the formaldehyde is virtually entirely desorbed from the sterile supplies. Therefore in most cases no additional degassing is needed.

3.3.2.3 Bioindicators

The test organism used for microbiological testing of FO sterilization processes is *G. stearothermophilus* NCTC 10003. Assembly of the bioindicator is described in ISO 11138.

3.3.2.4 In-process control

Recording of the pressure and temperature curve during the sterilization process.

Since in general bioindicators cannot be used in every batch to furnish proof of the sterilization results, at least chemical indicators, which undergo a change in colour, should be used to grant an insight into the effectiveness of sterilization.

For process control purposes, chemical indicators should be placed in a PCD as per EN 867-5 (Fig. 6) and then inserted into the items to be sterilized. Furthermore each item undergoing sterilization should be fitted with treatment indicators to demonstrate that the respective item was exposed to the sterilization gas (visual inspection).

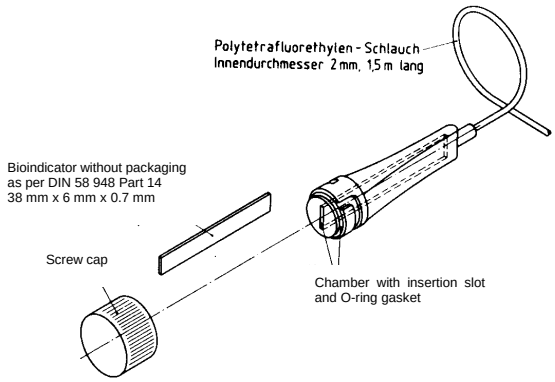

Fig. 6: Process challenge device as per EN 867-5

3.3.2.5 Verification of formaldehyde sterilization

Testing of formaldehyde sterilizers is regulated in EN 14180. The type test (which is generally performed by the manufacturer at the factory) serves to identify the operating data. Testing after installation (installation qualification) is carried out to demonstrate that the requirements set out in EN 14180 are being met. Periodic testing of the sterilizer is done to show that the sterilizer conducts sterilization in accordance with the operating instructions. To that effect, PCDs are used as per EN 867-5, but these contain bioindicators.

Routine testing should be performed at least quarterly in cooperation with an accredited microbiology laboratory. EN 14180 also calls for measurement of formaldehyde residues. (Requirements: mean value: 200 μg, peak value: 400 μg). Some older sterilizers are unable to meet these requirements, in such cases it is possible that the desorption phase will be prolonged.

3.3.2.6 Operation

The formaldehyde solution must be kept in a sealed, gastight container when stored. It should be stored at temperatures between 10 °C and 25 °C.

The sterile supplies must lend themselves to sterilization with formaldehyde (the manufacturer's instructions must be observed). In principle only items that do not tolerate steam sterilization may be sterilised with formaldehyde (heat-sensitive items). For cleaning, packing and loading the same guidelines apply as for ethylene oxide sterilization. The sterile supplies are immediately ready for reuse after completion of a sterilization process featuring effective steam purging. When storing the sterile supplies one must bear in mind that the sterile supply packaging may have absorbed formaldehyde and that this can be released again into the ambient air. Therefore compliance with the MAC values for formaldehyde in the storage rooms should be monitored.

The same maintenance guidelines apply for FO sterilizers as for EO sterilizers.

3.4 Hydrogen peroxide sterilization

(Example)

3.4.1.1 Method of action

The free radicals thus generated bind with functional cell components of microorganisms, irreversibly damaging them. After expiry of the exposure time the high-frequency field is switched off and hydrogen peroxide plasma is broken down to oxygen and hydrogen.

The process comprises a:

- ⇒ vacuum phase
- ⇒ injection phase (a small amount of hydrogen peroxide is injected)
- ⇒ plasma phase
- ⇒ aeration phase

3.4.1.2 Requirements for the medical devices to be sterilized

Items whose surfaces are easily accessible can be sterilized with the plasma process. Narrow-lumened instruments that are closed at one end cannot at all be sterilized with the plasma process. Nor do highly porous supplies such as cotton, waste, foam material or paper lend themselves to plasma sterilization. As well the process is not approved for implants.

As in all gas sterilization processes, supplies must be meticulously prepared before sterilization. The process is particularly susceptible to any residual soils (that will have persisted after cleaning and disinfection), hence even the presence of any salt crystals on the supplies could jeopardize the success of sterilization. This holds true especially for protein residues, etc. In the plasma process humid sterile supplies will make it impossible to attain the requisite low pressure values in the vacuum phase and thus lead to abortion of the sterilization cycle. As well it is of importance that the devices to be sterilized are totally dry. The nature of the process means that only special foil (Tyvek®) packaging can be used for the sterile supplies.

3.4.1.3 Testing and validation

Microbiological testing of sterilizers is conducted using PCDs provided by the manufacturer, with *Geobacillus stearothermophilus* as test organism. Currently H_2O_2 plasma sterilization processes can only be validated on the basis of microbiological methods, which is an onerous procedure. Parametric verification or release is not possible at present.

3.5 Sterilization with ionizing radiation

This kind of sterilization method is not used in hospitals but as an industrial method for e.g. single use devices.

In sterilization with ionizing radiation a distinction is made between particle beams (beta or electron beams) and electromagnet waves (gamma beams) based on their action.

The activity of ionizing radiation resides in its excitement, radical formation and ionization of atoms and molecules. These free radicals and excited or ionized atoms are highly reactive and kill any microorganisms present in the sterile supplies.

Both electron beams (less penetration depth) and gamma beams are used for sterilization.

In view of the high investment costs associated with these systems, such sterilization processes are used only in the industrial setting. The main application field is sterilization of medical single-use devices, pharmaceutical products as well as medical transplant materials.

Since this process is of no relevance for sterilization of reusable medical devices it shall not be elaborated on further here.

4 References

(1) Applicable CEN and ISO Standards

(2) Kramer, A und Assadian, O. (Hrsg.): Wallhäußers Praxis der Sterilisation, Desinfektion, Antiseptik und Konservierung. Georg Thieme Verlag, Stuttgart New York 2008.

(3) Bodenschatz W. (Hrsg.): Handbuch für den Desinfektor in Ausbildung und Praxis; Gustav Fischer Verlag, Stuttgart, 1993

(4) Robert-Koch Institut Berlin: Anforderungen der Hygiene bei der Aufbereitung von Medizinprodukten. Bundesgesundheitsbl 2012 • 55:1244–1310 © Springer-Verlag 2012

(5) http://www.cdc.gov/niosh/docs/81-123/pdfs/0293.pdf

(6) http://www.cdc.gov/niosh/docs/2007-164/pdfs/2007-164.pdf

Furthermore, technical documentation and information from various companies and research institutes were used.

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