Ref: **Device:** **Date:**

Manufacturer:				
Auditor:	Name		**Signatur:**	

1. Scope

This checklist is applicable for sterilization processes for medical products carried out with ethylene oxide. It shall be used for auditing operators of the corresponding sterilization equipment.

Where sterile products are to be included in the company's product spectrum, a sterilization assessment (including assessment of design and validation of sterilization processes) must be carried out based on at least one product file of a sterile product. For sterile products of risk class III, the documentation of design and validation must be examined.

Where an assessment of sterilization procedures validation is necessary as a part of the QM assessment for medical products, the present checklist should be applied in case of ethylene oxide used as the sterilizing agent.

2. Responsibilities and authority

Lead auditor

The lead auditor is responsible for the examination and evaluation of the QM system in respect of the customer's system documentation, the related standards and the ruling according to ISO 13485 and/or the Council Directive 93/42/EWG.

He is responsible for the work of the audit team and for the observance of the DQS processes. In case where the lead auditor is not a technical expert himself, he should accept the evaluation of the sterilization validation by the technical expert without any protest.

Technical expert

The expert is responsible for the competent evaluation of the aspects of the QM system that are specific for a product or a procedure. The assessment of the design documentation, especially those parts specifying the design and validation of sterilization procedures, is his essential task.

3. Approach to the evaluation

The goal of the assessment is to examine whether the requirements of ISO 11135-1 are fulfilled, or the satisfactory sterilization with ethylene oxide is evidenced in any other way. Any alternatively allowed procedure designated as such by the ISO 11135-1 shall be accepted.

The present checklist must be used as an appliance for the assessment.

The assessment results must be formulated in the audit report, where a reference to this checklist can be made.

4. Further applicable documents

. Technical file review

Assessment guideline

DIN EN ISO 11135-1 — Sterilization of health care products - Ethylene oxide - Requirements for design, validation and routine control of a sterilization process for medical devices

and other further applicable standards referenced.

5. Application of the assessment checklist

The checklist serves for the evaluation of audit results. Every audit requirement should be evaluated separately.

The evaluation of the documentation and implementation of a standard's requirement should be documented in the column "Evaluation" in the following way:

1 = fulfilled
2 = partially fulfilled, still acceptable
3 = partially fulfilled, not acceptable
4 = not fulfilled
na = not applicable

The numbering of the questions corresponds to the numbers of the requirements as printed in ISO 11135-1.

6. Audit protocol

Please use the DQS form "Findings" ("Feststellungen"). The findings must contain a reference to the checklist questions. These can be entered in the column "Reference" ("Referenz"). Please use the numbering system of the standard using at least two digits of the requirement's number (e.g. 4.2 for "Management Responsibility" associated with ISO 11135-1). Additional evidence, such as copies of manufacturer's documentation, should be ordered clearly (e.g. using the numbers).

7. Abbreviations

SAL	sterility assurance level
IQ	installation qualification
OQ	operation qualification
PQ	performance qualification
EO	ethylene oxide

No.	*Question*	*Evaluation*

Ref: **Device:** **Date:**

No.	*Question*	*Evaluation*

4 Quality management systems

4.1 Documentation

4.1.1	Have procedures for the design, validation, routine control and product release from sterilization been specified?	
4.1.2	Are all documents and records that are necessary according to ISO 11135-1 reviewed, approved and controlled*) by the designated personnel (see 4.2.1)?	

4.2 Management responsibility

4.2.1	Are responsibilities and authorities for all the requirements of ISO 11135-1 specified and assigned*) to qualified persons?	
4.2.2	Is there a contract agreement about the responsibilities and authorities, in case several organizations (with separate quality management systems) are involved?	

4.3 Product realization

4.3.1-4.3.2	Are procedures for purchasing, identification and traceability*) specified?	
4.3.3	Is a system for calibration of all equipment and testing instruments specified**)?	

4.4 Measurement, analysis and improvement — Control of nonconforming product

4.4	Are procedures for the control of nonconforming products, corrections, corrective actions and preventive actions specified*)?	

*) according to the applicable parts of ISO 13485

**) according to the applicable parts of ISO 13485 or ISO 10012

5 Sterilizing agent characterization

5.1 Sterilizing agent

5.1	Are the composition, storage conditions and storage length specified for the sterilizing agent? [Ethylene oxide (EO) or a mixture of EO with a diluting agent.]	

Ref: **Device:** **Date:**

No.	*Question*	*Evaluation*
5.2	**Microbicidal effectiveness**	
5.2	Is the microbicidal effectiveness being worked out, in case of an application of the EO composition or the diluting agent other then corresponding to the widely accepted conditions?	
5.3	**Material effects**	
5.3	(Assessment of the effects on the product according to Section 7)	
5.4	**Environmental considerations**	
5.4.1	Are there documented ▪ evaluation of the possible environmental effects? ▪ specified actions for the environmental protection? ▪ specified monitoring actions (where necessary)?	
5.4.2	Are applicable local / national / international regulations regarding emission and disposal of EO and its dilution agents being observed?	
6	**Process and equipment characterization**	
6.1	**Process**	
6.1.2	Does the process characterization include:	
	a) preconditioning (where applied)?	
	b) sterilization cycle?	
	c) ventilation (where applied)?	
6.1.3	Does the sterilization cycle include:	
	a) air removal?	
	b) conditioning (where applied)?	
	c) addition/admittance of EO?	
	d) maintenance of the specified conditions during application time?	

Ref: **Device:** **Date:**

No.	*Question*	*Evaluation*
	e) the removal of EO?	
	f) rinsing (where applied)?	
6.1.4	Is the (pre)treatment of the product with preconditioning and/or conditioning in order to achieve the specified temperature and humidity in the loading being carried out under controlled conditions? Is the humidity used for this purpose being produced from the admitted vapor?	
6.1.5-6.1.6	Is the range of every process variable (amongst others: temperature, humidity, EO concentration, pressure or vacuum, time) being specified and documented incl. their tolerances and means of monitoring?	

6.2 Equipment

6.2.1	Is the specification for the equipment to be used being developed and documented, incl. the area for the preconditioning and ventilation?	
6.2.2	Does the equipment specification include:	
	a) the equipment description, incl. all additional devices and manufacturing materials?	
	b) the composition of the sterilizing agent gases and further substances allowed in the sterilization chamber together with it?	
	c) the description of the gases and further substances allowed in the sterilization chamber together with them?	
	d) the vapor's quality and purity in order to assure its suitability for the equipment and products?	
	e) the description of the instruments for monitoring and recording of the sterilization process incl. the key parameters and measuring points?	
	f) the errors that are recognized by the equipment?	
	g) safety measures incl. the protection of environment and personnel?	
	h) requirements for the placing into operation (incl. monitoring of the emissions, if appl.)?	
6.2.3	Is there a documented evidence of correspondence with the specification for the software used for controlling and monitoring of the process? (Requirements for manufacturing and validation → ISO 9000-3)	

Ref: **Device:** **Date:**

No.	*Question*	*Evaluation*
6.2.4	Have measures been taken to make sure that a failure of the control function does not lead to a failure of the recording function, which could cause an inefficient process to be reported as being efficient?	

7 Product definition

7.1 General

7.1.1	Are actions taken to define the product before introducing a new or changed product, new packing or new loading configuration?	
7.1.2	Are evidences of equivalence with a previously validated product / packing / loading configuration being taken into account and is every evidence being documented?	
7.1.3-7.1.4	Are the permeation and removal of the humidity and EO made possible in the parts of product or packaging, that are most difficult to sterilize?	
7.1.5	Has the efficiency of the specified sterilization process been proven for the product parts that are most difficult to sterilize?	

7.2 Product safety and performance

7.2.1	Has it been proven that the specified sterilization process does not impact the orderly function of the product?	
7.2.2	Has the influence of multiple sterilization (if allowed) on the product and its packing been evaluated? (→ISO 17664)	
7.2.3	Is the biological safety of the product according to ISO 10993-1 and any applicable successive parts of ISO 10993 been determined?	
7.2.4	Do the EO residue concentrations in the products remain under the established limits (→ maximally allowed limits for residues acc. to ISO 10993-7)?	
7.2.5	Has it been confirmed that the product meets its specified requirements for safety, quality and performance after being exposed to the strongest process parameters?	

7.3 Microbiological quality

7.3.1	Is there a documented system assuring that the condition of the product to be sterilized is controlled and the efficiency of the sterilization process is not affected?	
7.3.2	Has the efficiency of this system been proven, incl.	

Ref: **Device:** **Date:**

No.	*Question*	*Evaluation*
	▪ an estimation of the bioburden according to ISO 11737-1 in specified periods (for single use products)?	
	▪ an evaluation of the efficiency of specified cleaning and (if applicable) disinfection procedure and an evaluation of organic and inorganic impurities (for reusable medical products, → ISO 17664)?	

8 Process definition

8.1	Is the sterilization process to be validated, specified and documented prior to introducing a new or changed product, packing or loading configuration?	
8.2	Is the sterilization chamber to be used for the process definition being put through the IQ and PQ (→next section)?	
8.3	Is the sterilization process to be applied to a defined product specified?	
8.4	Is the validity of process parameters incl. tolerances according to specification being supported by documentation and records?	
8.5	Has the microbial effectiveness of the sterilization cycle been determined by one of the methods described in the Annexes A or B, or with an alternative validated method evidencing the necessary SAL?	
8.6	Are the engaged biological indicators:	
	a) Indicator comply with ISO 11138-2 caluse 5 and 9.5	
	b) at least as resistant against EO as the bioburden?	
	c) evaluated at the points of the products, where attainment of sterilization conditions is most difficult, **or** being positioned in a process challenge device (PCD), for which the evidence of its suitability and the relationship to the parts of the product, that are most difficult to sterilize, is established and documented?	
8.7	Did the biological indicators comply with ISO 11138-1?	
8.8	Do the chemical indicators used meet the requirements of ISO 11140-1 and the applicable successive parts of ISO 11140?	
8.9	Do the sterility examinations comply with ISO 11737-2?	

Ref: **Device:** **Date:**

No.	*Question*	*Evaluation*

9 Validation

9.1 Installation qualification (IQ)

9.1.1	Does the IQ supply an evidence of sterilization equipment's compliance with their specification, incl. additional devices (Section 7) at the point of its delivery and installation?	
9.1.2	Is the complete specification for the EO allowing devices incl. any additional devices established and documented?	
9.1.3	Are the working conditions for the equipment specified and are at least the following procedures established:	
	a) step by step instructions manual?	
	b) error status, method of error indication, actions to be taken?	
	c) instructions for maintenance and calibration?	
	d) information on contact and technical support?	
9.1.4	Is there an established specification for the installation site including any necessary customer services and are all special preventive actions and measures known?	
9.1.5	Are the instructions for beginning of operation documented and do they include instructions concerning heath care and safety of the personnel?	
9.1.6	Are technical schemes of the equipment, sanitary supplies and other additional devices being completed during the IQ?	

9.2 Operation qualification (OQ)

9.2.1	Does the OQ prove the ability of the installed equipment to perform the specified processes within the specified tolerances (section 8)?	
9.2.2	Has the calibration of all the measuring and testing devices been confirmed prior to OQ? (4.3.3)	

Ref: **Device:** **Date:**

No.	*Question*	*Evaluation*
9.3	**Performance qualification (PQ)**	
9.3.1	**General**	**1.**
9.3.1.1	Is the PQ being carried out if there are new or changed products, packaging, loading configuration, equipment, process parameters, or is evidence of their equivalence with previously validated packaging, product, loading configuration, etc. being documented?	
9.3.1.2	Are products being used for the PQ?	
	Does the PQ bring an evidence of equipment's consistent function according to the previously defined criteria, and that the process delivers sterile products?	
9.3.1.3	Are the following aspects being observed during the conduction of PQ:	
	▪ loading configuration equivalent with the loading configuration in the routine process?	
	▪ use of the loading composition that is most difficult to sterilize?	
	▪ regular evaluation that the loading is suitable for validation?	
	▪ use of products / materials that are representative of those sterilized routinely?	
	▪ in case of reuse of a PQ loading: sufficient airing between the treatments?	
9.3.1.4	Is there a specification for the way of products' submission for sterilization?	
9.3.1.5	(See 8.7)	
9.3.2	**PQ — microbiological**	
	Are the following aspects being observed during the conduction of the microbial PQ::	
9.3.2.1	▪ conduction of the studies in a chamber for manufacturing?	
	▪ setup of the process parameters, so that the microbial effectiveness is lower then it is in the defined sterilizing process?	
9.3.2.2	▪ process parameters remaining within their specified limits (EO concentration, temperature, humidity)?	
9.3.2.3	▪ confirmation of the microbial effectiveness of the specified process for the given combination product / loading configuration?	

Ref: **Device:** **Date:**

No.	*Question*	*Evaluation*
9.3.2.4	▪ estimation of the microbial effectiveness with an approach described in the Annexes A or B of ISO 11135-1 or with another validated approach, for which there is an evidence of the required SAL?	
9.3.2.5	▪ where the process has been defined in a testing chamber — at least three reduced process runs in a production sterilizer in order to confirm the data gained in the testing chamber?	
9.3.2.6	▪ for the equipment of the same establishment, for which the IQ and OQ had been carried out and therefore only a reduced PQ is being conducted, — is there a documented justification of the PQ reduction with an evidence of the required levels of microbial effectiveness?	

9.3.3 PQ — physical

	Are the following aspects being confirmed / observed during the conduction of the physical PQ:	
9.3.3.1	▪ three consecutive assessment runs fulfilling all the acceptance criteria?	
9.3.3.2 a	▪ temperature and humidity within the specified ranges at the end of preconditioning (where applied)?	
9.3.3.2 b	▪ suitability of the specified maximal delay between the end of preconditioning and the beginning of the sterilization cycle?	
9.3.3.2 c	▪ an evidence that the allowance of EO gas into the chamber takes place?	
9.3.3.2 d	▪ quantity / concentration of the used EO in the chamber within the specified ranges?	
9.3.3.2 e	▪ temperature, humidity and, if appl., other process parameters in the chamber within their ranges according to the process specification?	
9.3.3.2.f	▪ Temperature is during the exposure time within the specified temperature range.	
9.3.3.2 g	▪ sterilizing loading being exposed to the temperature within the specified range during airing (where applied)?	

9.4 Changes to the loading configuration

9.4	Where the loading configurations are widely changing, is there an evaluation of the impact from these changes on the sterilization process? Is there an evidence that the required SAL is being achieved?	

Ref: **Device:** **Date:**

No.	Question	Evaluation
9.5	**Review and approval of validation**	
9.5.1	Does the PQ deliver a documented confirmation of the validation data against the recognized working instruction for the sterilization process, and is the process specification being confirmed?	
9.5.2	Is the acceptability being proven for the indications of the product definition, process definition as well as IQ, OQ and PQ, including the test results from the biological indicators? Are there records about this?	
9.5.3	Is the validation report being examined and released by the designated responsible persons?	
9.5.4	Does the validation report include the following statements:	
	▪ description of the given validated product, incl. the defined treatment configuration and the documented specification for the sterilization process with EO?	
	a) for the preconditioning, where applied:	
	1) treatment time, temperature and humidity in the chamber / area?	
	2) the allowed minimal temperature for the acceptance of preconditioning?	
	3) temperature and humidity of the loading to be sterilized?	
	4) the maximal delay between the withdrawal from the preconditioning and the initiation of sterilization?	
	b) for the conditioning, where applied:	
	1) quality of the starting vacuum (where applied) and the time necessary for its attainment?	
	2) time of exposure to vacuum?	
	3) application time, temperature, pressure and humidity in the chamber?	
	4) temperature and humidity of the loading?	
	c) for the exposure to EO:	
	1) pressure build-up during EO allowance, time of EO allowance, end pressure?	

Ref: **Device:** **Date:**

No.	*Question*	*Evaluation*
	2) EO concentration determined independently of the pressure build-up, incl. the indication of one of the parameters — EO weight, EO volume, direct measurement of the EO concentration in the chamber?	
	3) temperature in the chamber?	
	4) exposure time?	
	5) temperature of the loading?	
	6) confirmation of the operation for the gas circulation system (where applied) during the sterilization?	
	d) for the airing (where applied):	
	1) time and temperature?	
	2) pressure changes in the chamber / area?	
	3) transfer rate of the air / other gas?	
	4) temperature of the loading?	
	5) loading configuration and detachment of the products in the chamber / area?	
9.5.5	▪ additionally for the parametric release (if necessary):	
	a) humidity in the chamber incl. tolerances, measured directly during the conditioning?	
	b) EO concentration incl. tolerances, by direct analysis of the chamber atmosphere in specified periods, that are enough for the verification of the required conditions?	
	c) a designation concerning the satisfactory function of the gas circulation system (where applied) in the chamber during the exposure?	
9.5.6	Is the process specification being confirmed incl. its process parameter and their tolerance values? Does it include criteria allowing to recognize the conformance of an individual sterilization process for the application to a designated product/material to be sterilized?	

10 Routine monitoring and control

10.1	Are there following data recorded and retained for each sterilization cycle, which provide an evidence for observance of the sterilization process specification:

Ref: **Device:** **Date:**

No.	*Question*	*Evaluation*
	a) achievement of the necessary minimal temperature during preconditioning, if applied?	
	b) monitoring / recording of the temperature and humidity in the area of preconditioning, if applied?	
	c) for the preconditioning, if applied — the times of beginning and withdrawal of the loading?	
	d) Note that the gas circulation system was working sufficient during the exposure time.	
	e) the elapsed time between the withdrawal from preconditioning (where applied) and beginning of sterilization	
	f) temperature and pressure in the chamber during sterilization?	
	g) Control of th the humidity during the conditioning phase	
	h) evidence of EO gas allowance in the chamber?	
	i) Pressure rise and quantity of the EO used or EO concentration in the chamber?	
	j) confirmation of operation for the gas circulation system (where applied)?	
	k) application time?	
	l) Conditioning time	
	m) for the ventilation (where applied): time, temperature, pressure changes (where present), operation of the air supply (where applied)?	
	n) conformance of the biological indicators (8.6)?	
	o) conformance of the chemical indicators (8.8)?	
10.2	▪ additionally for the parametric release:	
	a) temperature measured on at least two points inside the chamber during the whole sterilization cycle?	
	b) EO concentration in the chamber, determined by the direct analysis of the chamber atmosphere throughout the complete exposure time in specified periods that are enough for the verification of the required conditions?	
	c) humidity in the chamber, measured directly during the preconditioning?	

Ref: **Device:** **Date:**

No.	*Question*	*Evaluation*
11	**Product release from sterilization**	
11.1	Are there documented criteria for recognizing the conformity of a sterilization process for application to a specific material to be sterilized:	
	a) confirmation of conformity of the data records during a routine sterilization with the specification of the sterilization process?	
	b) confirmation that there is no growth of the testing germs of the biological indicators (where applied)?	
11.2	Is the product identified as nonconforming and handled according to the applicable parts of ISO 13485, if one of the following requirements is not met? a) All process variables within the specified tolerances. b) Where biological indicators are being applied — no growth of the testing germs after the incubation.	
12	**Maintaining process effectiveness**	
12.1	**General**	
12.1.1-12.1.2	Is the consistent efficiency being proven periodically for the system, which assures the condition of products to be sterilized (7.3.1) and the accuracy and reliability of the measuring instruments for controlling and monitoring of the sterilization process being verified periodically (4.3.3)?	
12.2	**Maintenance of equipment**	
	Are the following aspects being observed during the maintenance:	
12.2.1	▪ planning of the preventive maintenance and its conduction according to documented procedures?	
12.2.2	▪ prevention of usage of the equipment until all maintenance tasks have been completed with a satisfactory result and recorded?	
12.2.3	▪ retention of the maintenance records?	
12.2.4	▪ regular documented assessment of the maintenance plan, procedures and records by a designated responsible person?	

Ref: **Device:** **Date:**

No.	*Question*	*Evaluation*
12.3	**Reassessment**	
12.3.1	Is there a documented reassessment of the sterilization process being carried out periodically for the specified equipment? Is there a documented procedure for it?	
12.3.2	Is there a documented check-up whether and to what extent is a reassessment of IQ, OQ and PQ necessary?	
12.3.3	Is biological indicators' suitability for use being examined in specified periods with respect to their bioburden (8.6)?	
12.3.4	Is there a documented estimation of suitability for the loading and its configuration?	
12.3.5	Is the validated process reassessed in every case, if a change is made to the sterilization equipment or to the product, which could impact the process efficiency?	
12.3.6	Is an investigation of the reason for an unsuccessful reassessment / routine monitoring result carried out, and the unsuitable process changed, so that the required SAL can be achieved?	
12.3.7	Are there records, reports, etc. about the evaluation of reassessment data, and correction action plans (if any) being retained?	
12.3.8	Are the following additional requirements being observed, if the parametric release is being applied:	
	a) sterilization process reassessment at least yearly?	
	b) a confirmation of the achieved SAL by microbiological studies as a part of reassessment?	
12.4	**Assessment of change**	
12.4.1	Is every change to the equipment / product / packaging / products submission for sterilization / sterilizing agent or its application being evaluated in respect to its influence on the effectiveness of the sterilization process?	
12.4.2	Does the definition of the validation's extent (IQ, OQ, PQ) take into account the dimension of the change?	
12.4.3	Is there a definition for the extent of the evaluation of a change? Is the evaluation being documented, incl. a justification of decisions taken?	