This checklist is **not** intended for use with *terminally sterilized* or *re processable medical devices sterilized by H2O2 Gas Plasma*. Please use the more specific checklists for H2O2 terminally sterilized devices ([MED\_T\_09.81](https://roxtra.tuev-sued.com/Roxtra/doc/showfile.aspx?FileID=208226)) or re-processable devices using H2O2 ([MED\_T\_09.82](https://roxtra.tuev-sued.com/Roxtra/doc/showfile.aspx?FileID=208228)) and request a current copy from your TÜV SÜD Product Service primary point of contact.

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| **Application ID (as it appears in the application form / change notification form)** |
|  |

* *[X]* in this document: indicates a document to be named including page number - submitted for evidence. Grey text (for guidance) may be replaced/deleted.
* In case of a Change Notification, please only fill in the applicable sections

# Short Product Description relevant to the sterilization process

*Note: Please replace grey italic text with respective information*

|  |
| --- |
| **Short description incl. picture of the device** - in case of changes, as far as relevant |
| Description of the device as far as relevant for sterilization (pictures for clearer understanding):*To be added**Product Schematic and / or Photo of product, size, material, Intended Use / Intended Purpose according to IFU (inclusive total application duration, body contact, implantable, patient group), Packaging description, Picture*Variants under assessment: *To be added**Product variants (e.g. Same product in different SBS, Multiple products in same SBS)**Description of the Sterile Barrier System Specifications used at sterilization** *What is the representative / worst-case SBS for the product under assessment?*
 |

|  |
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| **Manufacturing facility and certification status of the applicable sterilization sites / facilities** |
| *(Product) Manufacturing site(s) to be named* | *Please provide the applicable QMS Certificate 13485 of all applicable manufacturing site(s), if not already listed on the certificate.* |
| *Sterilization site / Validation contractor* | *Please provide the applicable QMS Certificate 13485 of the used sterilization site**In case of identical laboratory subcontractor (e.g. residual analysis, microbial testing) please additionally provide ISO 17025 certificate including respective scope.**In case the sterilization site and the H2O2 sterilization study provider are not identical, please provide respective information for all involved parties.* |
|  |  |

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| **External laboratories if used for sterilization validation and certification status of the laboratory** |
| *Name of the laboratory* | *Please name the test done by the laboratory (e.g. Microbiology BI testing, Sterility testing, Bioburden, Residuals). Please provide the applicable QMS Accreditation Certificate (e.g. ISO 17025 or GLP)*  |
| *Name of the laboratory* | *Please name the test done by the laboratory (e.g. Microbiology BI testing, Sterility testing, Bioburden, Residuals). Please provide the applicable QMS Accreditation Certificate (e.g. ISO 17025 or GLP)* |
|  |  |

# Production related Information

## Used Hardware Specifications

*Note: Please replace grey italic text with respective information. Please add additional lines if required.*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Equipment including Identifier (e.g. int. ID/ serial number & software revision)** | **Site / Location** | **Applicable cycle operated by the equipment for the device in question** | **Typical load configuration** | **Usable chamber volume in m3** | **All sensors / measurement devices (internal + external sensors, dataloggers for validation) are calibrated** |
| *e.g. Formaldehyde Low Temp* | *Inhouse or external source* | *Please name the cycle and Version/ Revision of cycle**e.g. Super CLEAN**please list ALL cycles that are intended to be used together with the product, e.g. 55°C / 60°C & 70°C using 27% formaldehyde* | *e.g. Flexible Endoscope / Central Sterilization mixed load* | *5,4* | [ ]  Yes[ ]  No |
|  |  |  |  |  |  |

*Notes:*

* *Sensor calibration and equipment maintenance need to cover all critical sensors, e.g. optical / spectral detector for the sterilizing agent in-process monitor.*
* *Sterilizer equipment used for the validation must be CE certified by a European Notified Body. In any other case a full sterilizer equipment design documentation needs to be submitted to be reviewed additionally.*

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| **Sterilizing agent definition** |
| *What is the sterilizing agent and how is it presented to the sterilizer / sterilization process?* | *Further details on the sterilizing agent presentation: Half-Dose cartridge, Booster, 3rd party cartridge, canister, container, bottle, fill volume, sample picture, REF Code or order code from supplier, other unique identifier, certificate of conformity or certificate of analysis**In case of different presentations (e.g. 3ml cartridge & 10ml cartridge) please use a new row for each presentation* |
|  |  |

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| --- |
| **Accessories & Components (necessary & optional) as part of the validation and routine processing** |
| *Please list all accessories and components that are to be used in preparation and/or inside the sterilization chamber for the validation activities and also for intended routine sterilization.** *SuperFOIL Sterilization Wrap*
* *Chemical indicator Tape 🡪 Chemical indicators need to be compliant to EN ISO 11140-1*
* *Special bags / trays / accessories by the equipment manufacturer*
* *Special probes / indicators / sensors that are used in the sterilization cycle and may determine the cycle outcome or deliver relevant information to the cycle decision of OK / NOK.*
 |

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| **Biological Indicator (BI) / Process Challenging Device (PCD) description** |
| *Minimum expected level of information:** *Detailed description of the BI (carrier material, dimensions, microorganism, population, D-Value with respect to the sterilizing agent, survival/kill window, dose/response characteristics, adherence to EN ISO 11138-1, Certificate of Analysis, Certificate of Compliance)A full investigation study (including scientific data) needs to be provided to demonstrate equal or higher resistance of the chosen standard microorganism.If biological indicator is not sourced from a certified supplier (e.g. manufactured by internal microbiology lab), then a full design documentation of the BI manufacturing process needs to be added to the documentation or separately covered by a supplier audit of this manufacturing process.*
* *Detailed description of the PCD (picture / drawing, placement of BI inside PCD, inoculation with spore suspension)*
* *Is the used ePCD available in the market to the commercial end-user? If not, how is the correlation between the publicly available ePCD (for routine release) to the custom ePCD within this validation achieved?*
 |

## *If Applicable:* Cleaning of Product in Manufacturing before Sterilization

*Note: Please replace grey italic text with respective information. Please add additional lines if required.*

|  |
| --- |
| **Cleaning process description** |
| Are cleaning parameters that are specific for the medical device defined? | [ ]  yes documented in *[X,p.y]*  [ ]  no *please justify:*Please describe the cleaning process:*Parameters of the cleaning process may be specific load configuration, positioning, connection, accessories, process chemicals, pressures or temperature limit(s)…* |
| Have cleaning studies been performed at validation of the used equipment to approve the respective cleaning process step is able to deliver appropriate performance? | [ ]  yes documented in *[X,p.y]*  [ ]  no *please justify:**Cleaning studies shall reflect the potential contamination and evidence of reproducible elimination of the contamination to a safe level (see EN ISO 17664)* |
| Are process residuals within limits? | [ ]  yes documented in *[X,p.y]*  [ ]  no *please justify:**Residuals like endotoxins, particles, org. inorganic contaminations, detergent residues with adequate risk related to the device and body contact shall be safe and acceptable.* |
| Are preventive maintenance operations defined including frequencies? | [ ]  yes documented in *[X,p.y]*  [ ]  no *please justify:**Examples for preventive maintenance are: exchange of cleaning media and/or equipment* |
| Residual cleaning agent impact on sterilization process | *Please specify maximum allowable limits for residual cleaning agent on the device-to-be-sterilized that could adversely affect the subsequent sterilization cycle.**Only applicable if no disinfection step follows this cleaning step. Otherwise refer to the same question in the next section 2.3* |

## *If Applicable* - Disinfection of Product in Manufacturing before Sterilization

*Note: Please replace grey italic text with respective information. Please add additional lines if required.*

|  |
| --- |
| **Disinfection process description** |
| Are parameters that are specific for the medical device defined, such as specific load configuration, positioning, connection, accessories, process chemicals, pressures or temperature limit(s)? | [ ]  yes documented in *[X,p.y]*  [ ]  no *please justify:*Please describe the disinfection process:*Parameters of the disinfection process may be specific load configuration, positioning, connection, accessories, process chemicals, pressures or temperature limit(s)…* |
| Were disinfection studies performed at validation of the used equipment to approve the respective disinfection process step is able to deliver appropriate performance? | [ ]  yes documented in *[X,p.y]*  [ ]  no *please justify:**Disinfection studies shall reflect the potential contamination and evidence of reproducible elimination of the contamination to a safe level (see EN ISO 17664)* |
| Are process residuals within limits? | [ ]  yes documented in *[X,p.y]*  [ ]  no *please justify:**Residuals like endotoxins, particles, org. inorganic contaminations, detergent residues with adequate risk related to the device and body contact shall be safe and acceptable.* |
| Are preventive maintenance operations defined including frequencies? | [ ]  yes documented in *[X,p.y]*  [ ]  no *please justify:**Examples for preventive maintenance are e.g. exchange of disinfection media and or equipment* |
| Residual cleaning & disinfection agent impact on sterilization process | *Please specify maximum allowable limits for residual cleaning & disinfection agent on the device-to-be-sterilized that could adversely affect the subsequent sterilization cycle.* |

## Only applicable to *Change* of Clean Room Control / Validation

*Note: Please replace grey italic text with respective information. Please add additional lines if required.*

|  |  |
| --- | --- |
| Cleanroom | *Please identify the cleanroom(s) where the manufacturing takes place, including ISO classification* |
| Are action and alert levels/limits set appropriately for the subsequent product bioburden in cleanroom processes? | [ ]  yes documented in *[X,p.y]*  [ ]  no *please justify:*Acceptance criteria for “in operation” condition:Airborne particles [*size*]: particles/m3Airborne microbiological contamination: cfu/m3 *(and/or settle plates)*Surface microbiological contamination: cfu/ surface areaProduct bioburden: cfu *(type – spores, fungi, anaerobe, bacteria) The bioburden shall be known to a degree to make decisions on resistance* |
| Monitoring points are defined for the above-mentioned measurements | [ ]  yes documented in *[X,p.y]*  [ ]  no *please justify* |
| Was IQ, OQ, PO of the cleanroom successfully established? | [ ]  yes documented in *[X,p.y]*  [ ]  no *please justify:* |
| Is all measuring equipment in a calibrated state? | [ ]  yes documented in *[X,p.y]*  [ ]  no *please justify:* |
| Are utilities and media under surveillance | [ ]  yes documented in *[X,p.y]*  [ ]  no *please justify:**Please specify what media and related acceptance criteria are defined.**e.g. for water, compressed air…* |
| Are environmental parameters defined: | [ ]  yes documented in *[X,p.y]*  [ ]  no *please justify:*Please specify - where applicable:Temperature: Humidity:Pressure gradient/Pressure level at each room:Air change rates:Recovery rates |

## Cycle Specification

*Note: Please replace grey italic text with respective information for inhouse and outsourced processes. Please add additional lines if required.*

**Please paste copy of the cycle specification used at *routine* sterilization:**

|  |
| --- |
| *Please paste or reference [X] cycle specification here**In case modified parameters have been used during validation, please highlight the different parameters and provide a rationale for deviating from the routine cycle (see also section 2.9 for validation cycle specifications).**In case only pre-defined sterilization programs / cycles can be selected by the end-user, please provide a rationale and reference to the cycle descriptions in the equipment manufacturer’s manual.* |

|  |  |
| --- | --- |
| Is re-sterilization allowed? | [ ]  Yes*Please state the maximum number of allowed re-sterilizations of the product or product family under assessment.**How was this maximum number of possible re-sterilization cycles determined? Is a study available that supports this value?*[ ]  No |
| Was product functionality and residual limits verified after maximum amount of allowed sterilization cycles | *Besides product functionality testing please also consider the possible amount of* *sterilizing agent residues after a maximum amount of re-sterilization cycles*[ ]  Yes, documented in *[x]* [ ]  No, *please justify*: |

## Basic Validation Development Data

*Note: Please replace grey italic text with respective information.*

|  |  |
| --- | --- |
| Validation Method | [ ]   Overkill half cycle / partial cycle approach (EN ISO 14937 Annex D / Approach 3)[ ]   BI and bioburden (EN ISO 14937 Annex C / Approach 2)[ ]   Bioburden (EN ISO14937 Annex B / Approach 1)[ ]   Product adoption to an existing cycle:*Please assure that the adoption rationale and MPQ/PPQ validation data are submitted for the predicate device. This data is documented in [X]*[ ]   Other: *Please specify and add rationale for not using a standardized method* |
| Validation related Procedures | Procedures to be included as part of the submission:[ ]   How new product will be added to a sterilization cycle- *is documented in [X]*[ ]   By what events a new validation is triggered and what step of validation has to address what type of measurements - *is documented in [X]**Please provide the review interval of data, and interval of time till repeat MPQ PPQ studies. When was the last MPQ, PPQ study executed?**What are further criteria that trigger a revalidation study (e.g. Product changes…)?**Is a routine interval specified (e.g. annual requalification)?*[ ]   How new equipment/process will be qualified/validated - *is documented in [X]*[ ]  What significant changes related to sterilization will be notified to the Notified Body - *is documented in [X]*[ ]  Validation protocol for the actual sterilization cycle including acceptance criteria - *is documented in [X]* |

## OQ Operational Qualification

*Note: Please replace grey italic text with respective information for inhouse and outsourced processes. Please add additional lines if required.*

|  |  |
| --- | --- |
| Please list the governing critical physical / chemical parameters that need to be measured | *Below list is non-exhaustive and merely an example for possible key parameters to the sterilization cycle. Please adopt / extend to your specific sterilization process.** *Temperature*
* *Humidity*
* *Pressure*
* *Sterilizing agent concentration*
* *Vacuum level*
 |
| Please indicate the allowed tolerance band for each of the above critical process parameters | *Below list is non-exhaustive and merely an example for possible key parameters to the sterilization cycle. Please adopt / extend to your specific sterilization process.** *Temperature = 55°C +/- 5°C*
* *Sterilizing agent concentration range*
* *Pressure range*
* *Vacuum level range*
* *Humidity range*
 |
| Please outline the test schedule which is performed as OQ | *In this field, please list all tests which are performed to confirm that the sterilizing equipment is capable to adequately deliver the chosen process cycles within defined tolerances (EN ISO 14937:2009, section 9.3.).**The list below is non-exhaustive and merely presents an example** *Vacuum leak test (if applicable)*
* *Air removal challenge test, e.g. for devices with long lumen or where air needs to be removed to enable diffusion of the sterilizing agent.*
* *Temperature profile in empty chamber and representative min/max load🡪 Please state how many temperature probes are distributed within the chamber and load and where?*
* *Humidity profile in empty chamber and representative min/max load🡪 Please state how many humidity probes are distributed within the empty chamber and load and where?*
* *Sterilizing agent distribution in empty chamber and in representative min/max load.🡪 Please clearly describe how the distribution is measured and minimum required concentration is achieved throughout the load. This part may be executed together with MPQ to correlate minimum concentration to lethality.*
 |

## PPQ Physical Performance Qualification

*Note: Please replace grey italic text with respective information for inhouse and outsourced processes. Please add additional lines if required.*

|  |  |
| --- | --- |
| Please specify the validation load configuration: | Please specify the load used during validation at PPQ and MPQ:*Please consider min and max configuration in case of widely varying load configurations, scheme of total load), number of BIs, number of Sensors, scheme of position of BIs, total load volume, density, amount of adsorptive material. The data is documented in [X]* |
| Please specify which product was used in the load: | The product is the same as in section 1[ ]  yes    [ ]  no *– Please provide a description and justification*  |
| Results PPQ / Raw data | *Please provide a reference to the gathered PPQ data. This information could also have been already collected within OQ. In this case, please reference to the respective OQ results data for review [X]* |

## MPQ

*Note: Please replace grey italic text with respective information for inhouse and outsourced processes. Please add additional lines if required.*

**Please paste copy of the cycle specification used at *validation* of sterilization MPQ (e.g. half-cycle / partial cycle):**

|  |
| --- |
| *Please paste or reference [X] here. Cycle record summaries are documented in [X]**If identical to routine cycle as described / referenced in section 2.5, please specify.* |

|  |
| --- |
| **MPQ Processing - Microbial Performance Qualification** |
| Worst-case sterilizer conditions met? | *Please explain, how the worst-case sterilizer process limits have been challenged (e.g. using sterilizing agent at end-of-shelf-life, highest tolerable process pressure, lowest plasma power). Please only consider parameters, that are changeable by the equipment end-user.**This ensures that the sterilizer equipment, operating at the lower process limits, is still capable of achieving an SAL<10-6 in the chosen cycle for the device-under-test.* |
| Placement scheme of BI and/or PCD within the load and in/on the actual device | *Please provide detailed information where the BI / spore inoculation / PCD placement in or on the medical device is done, including a rationale (e.g. longest lumen, difficult to reach crevice, high absorbent material, high surface roughness, etc.)**Additionally, please provide the placement of BI/PCD within the chamber load to resemble routine conditions (load release).* |
| BI incubation conditions(Reduced Incubation Time RIT) | *If incubation duration is less than 7 days, please provide a reduced-incubation-time (RIT) study in a representative load (no manufacturer study in a BIER vessel) to substantiate the incubation time [X].* |
| BI results including culture conditions and time between end of cycle and BI testing | [ ]  BI results including culture conditions and time between end of cycle and BI testing is documented in *[X]* |
| Confirm resistance hierarchy from least resistant (natural product bioburden) < IPCD <= ePCD (most resistant) | [ ]   sublethal / reduced cycle for BI resistance was performed and is documented in [X][ ]  Data on the relationship of the resistance between ePCD, iPCD, worst-case Products, natural Bioburden is provided and is documented in [X]. |
| Material-dependent microbial resistance | *Please state how material-dependent microbial resistance is covered during the validation activity? It is well-known, that different material surfaces exhibit large variability in microbial inactivation time. Please consider the following** *What would be the worst-case material with respect to the sterilizing agent?*
* *Is this material covered / included by the validation activity?*
* *How is the material covered (e.g. direct inoculation on the actual device, BI using this material as carrier material, representative worst-case inoculated dummy material, etc.)*
* *Has this been pre-established by the equipment manufacturer in an internal study that could be referenced / audited?*
 |
| Pre-sterilization Bioburden | *Please specify the bioburden level and llimits e.g. in respect to bacteria, yeast/molds and anaerobic bacteria (were these investigations at least part of the initial assessment of bioburden)**Please provide the bioburden trending data as a summary of the past two (2) years, if not available at least for the validation LOT plus a rationale (e.g. manufacturing occurs only twice per year).**.* |
| Is endotoxin testing applicable for the device under assessment? | [ ]  no  [ ]  yes [X,p.y]*Please specify the method and related results. The data is documented in [X].* *(e.g. in case of direct contact to blood, CNS, eye or other systemic exposure)**If endotoxin monitoring is not required / not executed, please provide a detailed rationale.* |

# Sterilizing Agent Residuals (EN ISO 10993-17)

*Note: Please replace grey italic text with respective information for inhouse and outsourced processes. Please add additional lines if required.*

*Note: In case that test methods are qualified internally, a full review of the method qualification is required.*

|  |  |  |  |
| --- | --- | --- | --- |
|  |  |  | **Comments** |
| Was a full health-based risk assessment conducted and appropriate limits for residuals established  | [ ]  Yes, documented in *[X]* |  | *This is a minimum requirement, following the ISO 10993-17 and EN ISO 14937, clause 8.8* |
| Is a rationale provided for selection of representative sample(s) | [ ]  Yes, documented in *[X]* | [ ]  No, *please justify*: | *To be added if any*  |
| Are the applicable Allowable limits for the sterilizing agent residuals specified (including max. re-sterilization cycles) and confirmed for the product in question considering the patient population providede.g. by TCL, TI, TTC,  | [ ]  Yes, documented in *[x]* | [ ]  No, *please justify:* | *To be added if any*  |
| Results and Test method provided | [ ]  Yes, documented in *[x]* | [ ]  No, *please justify:* | *To be added if any*  |
| Are the used test methods validated? | [ ]  Yes, documented in *[x]* | [ ]  No, *please justify:* | *To be added if any*  |

# Routine Processing

*Note: Please replace grey italic text with respective information*

|  |
| --- |
| **Routine Processing** |
| Routine release | [ ]  BI and Physical load parameters*Placement scheme and number of BIs, Certificate of BI or spore suspension*[ ]  BI incubation time 7 days / 14 days?*If incubation duration is less than 7 days, please provide a reduced-incubation-time study in a representative load (no manufacturer study in BIER vessel) to substantiate the incubation time [X].*[ ]  Parametric release strategy provided in document [X]*Please provide a detailed parametric release investigation in order to demonstrate process robustness within the key process parameters, including the clear definition of tolerances / tolerance bands for each of the key process parameter. The study is presented in document [X]* |
| How is a successful process run established in routine process? | *Please describe or reference to a document, explaining how the standard sterilization process outcome is verified by the equipment and/or other utilities and finally established to meet the validated conditions from PPQ and MPQ?**Are sensory solutions used?**Are physical / chemical indicators used at worst-case positions or within PCDs to confirm successful process run?**Is a sample batch record available, please provide and reference respective document.* |
| Placement scheme and number of BIs, BI certificate provided? | [ ]  Yes, documented in *[x]*[ ]  No, *please justify:* |
| Load configuration | [ ]  Dedicated load *Product configuration is fixed in number and location within chamber*[ ]  Mixed load*different products allowed*Please add information on min/max load variation, if applicable: |
|  |  |

|  |
| --- |
| **Release by client:** |
|  |  |  |  |  |
| **Date** |   |  Signature |  | Full Name & Position |
|  |  |  |  |  |
|  |   |   |  | Name of Legal Manufacturer |

*Note as to the signature’s relevance: If this document is officially signed, the provided rationales and data herein*

*can be officially used by the reviewer. Otherwise, only the referenced documents can be used as evidence.*