Sterilization of health-care products — Ethylene oxide —Requirements for the development, validation and routine control of a sterilization process for medical devices

医疗保健产品灭菌—— 环氧乙烷——

医疗器械灭菌过程开发、确认和常规控制要求

1 Scope范围

1.1 Inclusions 包含内容

This International Standard specifies requirements for the development, validation and routine control of an ethylene oxide sterilization process for medical devices in both the industrial and health care facility settings, and it acknowledges the similarities and differences between the two applications.

本标准规定了医疗器械产品在工业与医疗保健机构的环氧乙烷灭菌过程的开发、验证和常规控制的要求，并承认这两个领域之间灭菌过程开发、确认的常规控制的异同。

NOTE 1. Among the similarities are the common need for quality systems, staff training, and proper safety measures. The major differences relate to the unique physical and organizational conditions in health care facilities, and to the initial condition of reusable medical devices being presented for sterilization.

注1. 其中，相同之处在于质量体系、人员培训及适当的安全措施的通用要求。主要的区别涉及到医疗保健机构的独特的硬件环境和组织条件，以及供灭菌的可重复使用医疗器械的初始条件。

NOTE 2. Health care facilities differ from medical device manufacturers in the physical design of processing areas, in the equipment used, and in the

availability of personnel with adequate levels of training and experience. The primary function of the health care facility is to provide patient care; medical device reprocessing is just one of a myriad of activities that are performed to support that function.

注2. 医疗器械制造商与医疗机构的主要不同点在于灭菌区域的硬件设计、所使用的设备，以及有技能和经充分培训的人员的可用性方面。卫生保健机构的基本功能是为病人提供医疗保健;医疗器械的再处理仅是支持医疗保健功能的无数活动之一。

NOTE 3. In terms of the initial condition of medical devices, medical device manufacturers generally sterilize large numbers of similar medical devices that have been produced from virgin material. Health care facilities, on the other hand, must handle and process both new medical devices and reusable medical devices of different descriptions and with varying levels of bioburden. They are therefore faced with the additional challenges of cleaning, evaluating, preparing and packaging a medical device prior to sterilization. In this International Standard, alternative approaches and guidance specific to health care facilities are identified as such.

注3. 就医疗器械的初始条件而言，医疗器械制造商通常灭菌大量的从原始材料开始生产的类似的医疗器械。另一方面，卫生保健机构必须同时处理和加工有着不同生物负载水平的新的医疗器械和再次使用的医疗器械。因此，医疗保健机构的灭菌产品面临着在灭菌前清洗、评估、准备和包装医疗器械的额外挑战。在本标准，确定了针对医疗保健机构的灭菌过程开发、确认和控制的方法或指南。

NOTE 4. EO gas and its mixtures are effective sterilants that are primarily used for heat- and/or moisture-sensitive medical devices that cannot be moist heat sterilized.

注4. EO气体及其混合物是一种主要用于对湿热敏感而不能用湿热进行灭菌的医疗器械灭菌的有效的灭菌剂。

NOTE 5. Although the scope of this International Standard is limited to medical devices, it specifies requirements and provides guidance that can be

applicable to other health care products.

注5 尽管本标准限定于医疗器械，但标准规定的要求和提供的指南同样适用于其他医疗保健产品。

1.2 Exclusions 不适用

1.2.1 This International Standard does not specify requirements for the development, validation and routine control of a process for inactivating the causative agents of spongiform encephalopathies such as scrapie, bovine spongiform encephalopathy and Creutzfeldt-Jakob disease. Specific recommendations have been produced in particular countries for the processing of materials potentially contaminated with these agents.

本标准没有对海绵状脑病的致病因子(如痒病、牛绵状脑病和克-雅病)的灭活过程的开发、确认和常规控制作出规定。有些国家已有了处理可能受此类因子污染的材料的推荐资料。

NOTE, See ISO 22442-1, ISO 22442-2 and ISO 22442-3.

注，见ISO 22442-1, ISO 22442-2 和 ISO 22442-3

1.2.2 This International Standard does not detail a specified requirement for designating a medical device as sterile.

本标准未详细论述确定医疗器械为无菌的规定要求。

NOTE Attention is drawn to national or regional requirements for designating medical devices as “sterile”. See for example EN 556－1 or ANSI/AAMI ST67.

须注意国家和地区确定医疗器械‘无菌’的要求，见如EN556-1或ANSI/AAMI ST67。

1.2.3 This International Standard does not specify a quality management system for the control of all stages of production of medical devices.

本标准未对医疗器械生产各个阶段的控制的质量管理体系作出规定。

NOTE The effective implementation of defined and documented procedures is necessary for the development, validation and routine control of a

sterilization process for medical devices. Such procedures are commonly considered to be elements of a quality management system. It is not a requirement of this International Standard to have a full quality management system during manufacture or reprocessing. The necessary elements are normatively referenced at appropriate places in the text (see, in particular, Clause 4). Attention is drawn to the standards for quality management systems (see ISO 13485) that control all stages of production or reprocessing of medical devices. National and/or regional regulations for the provision of medical devices might require the implementation of a full quality management system and the assessment of that system by a third party.

建立医疗器械灭菌过程的开发、确认和常规控制的文件化的，并能有效实施的程序是必需的，这样的程序文件通常被认为是质量管理体系的要素。在制造和再加工期间有一个充分的质量管理体系不是本标准的要求，必需的要素在接下来的适当地方(见第4章)被规范性引用。须注意控制医疗器械生产和再加工各个过程的质量管理体系的标准(见ISO13485)。国家和/或地区的法规可能对医疗器械质量管理体系及其第三方评价作出了规定。

1.2.4 This International Standard does not specify requirements for occupational safety associated with the design and operation of EO sterilization facilities.

本标准没有对与环氧乙烷灭菌机构的设计和与操作有关的职业安全要求作出规定。

NOTE 1 For further information on safety, see examples in the Bibliography. National or regional regulations may also exist.

注1，有关安全性的进一步的信息，请参阅‘参考文献’。国家或地区性法规也可能有明确规定。

NOTE 2 EO is toxic, flammable and explosive. Attention is drawn to the possible existence in some countries of regulations giving safety requirements for handling EO and for premises in which it is used.

注2，EO有毒，易燃，易爆。需注意，有些国家的法规可能对EO处理和使用场所的安

全要求作出了规定。

1.2.5 This International Standard does not cover sterilization by injecting EO or mixtures containing EO directly into packages or a flexible chamber.

本标准未覆盖用直接注射环氧乙烷或其混合气体到产品包装或活动柜室中的灭菌。

NOTE See ISO 14937 for these types of EO processes.

注，这些类型的EO灭菌过程见ISO 14937

1.2.6 This International Standard does not cover analytical methods for determining levels of residual EO and/or its reaction products.

本标准未覆盖测定EO残留和/或其反应物水平的分析方法。

NOTE 1 For further information see ISO 10993-7.

注1，EO残留的分析方法的进一步信息见ISO 10993-7

NOTE 2 Attention is drawn to the possible existence of national or regional regulations specifying limits for the level of EO residues present on or in medical devices.

注2，应注意,国家或地区的法规可能对医疗器械产品中环氧乙烷残留极限量作出了规定。

2 Normative references引用标准

The following documents, in whole or in part, are normatively referenced in this document and are indispensable for its application. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

以下参考标准,全部或部分，对本标准的应用是必不可少的。注明日期的标准，其引用版本适用；不注明日期的标准，其最新版本（包括修订）适用。

ISO 10012, *Measurement management systems — Requirements for measurement processes and measuring equipment*

ISO10012，测量管理系统——测量程序和测量设备的要求

ISO 10993-7, *Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals*

ISO10993-7医疗器械的生物学评价--第7部分:环氧乙烷灭菌残留量

ISO 11138-1:2006, *Sterilization of health care products — Biological indicators — Part 1: General requirements*

ISO11138-1：2006 医疗保健产品灭菌 生物指示物 第1部分：通则

ISO 11138-2:2009, *Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes*

ISO11138-2：2009 医疗保健产品灭菌 生物指示物 第2部分：环氧乙烷灭菌用生物指示物

ISO 11140-1, *Sterilization of health care products — Chemical indicators — Part 1: General requirements*

SO11140-1 医疗保健产品灭菌 化学指示剂 第1部分：总要求

ISO 11737-1, *Sterilization of medical devices — Microbiological methods — Part 1: Determination of a population of microorganisms on products*

ISO11137-1医疗保健产品灭菌 微生物方法 第1部分：产品微生物数量的测定

ISO 11737-2, *Sterilization of medical devices — Microbiological methods — Part 2: Tests of sterility performed in the definition, validation and maintenance of a sterilization process*

ISO 11737-2, 医用器械的灭菌 微生物学方法 第二部分：确认灭菌过程的无菌试验

ISO 13485:2003/Cor 1:2009, *Medical devices — Quality management systems — Requirements for regulatory purposes — Technical Corrigendum 1*

ISO 13485:2003/Cor 1:2009, 医疗器械 质量管理体系 常规要求 技术勘误

3 Terms and definitions 术语和定义

For the purposes of this document, the following terms and definitions apply.

本标准使用以下术语和定义

3.1 Aeration 通风

part of the sterilization process during which ethylene oxide and/or its reaction products desorb from the medical device until predetermined levels are reached

灭菌过程的一部分，环氧乙烷和/或其反应产物从医疗器械解吸附至预定水平的过程。

Note 1 to entry: This can be performed within the sterilizer and/or in a separate chamber or room.

注1，可在灭菌器中进行，也可在单个柜室或房间内进行。

3.2 aeration area 通风区

either a chamber or a room in which aeration occurs

发生通风的柜室或房间。

3.3 Bioburden 生物负载

population of viable microorganisms on or in product and/or sterile barrier system

[SOURCE: ISO/TS 11139:2006, definition 2.2]

产品和/或无菌屏障系统表面或内部的活的微生物数量。

[依据：ISO/TS11139：2006，定义2.2]

3.4 biological indicator 生物指示剂

test system containing viable microorganisms providing a defined resistance to a specified sterilization process

[SOURCE: ISO/TS 11139:2006, definition 2.3]

对特定灭菌过程具有确定抗力的染菌测试系统。

[依据：ISO/TS11139：2006，定义2.3]

3.5 Calibration 校准

set of operations that establish, under specified conditions, the relationship between values of a quantity indicated by a measuring instrument or measuring system, or values represented by a material measure or a reference material, and the corresponding values realized by standards

[SOURCE: ISO/TS 11139:2006, definition 2.4]

用已知精度(可追溯到国家标准)的测量系统或器具与未知精度的测量系统或器具进行比较，以检测、对比、报告或通过调整来消除未检定测量系统或器具对所要求的性能极限的任何偏差。

[VIM1993，定义6.11]

3.6 chemical indicator 化学指示剂

test system that reveals a change in one or more pre-defined process variables based on a chemical or physical change resulting from exposure to a process

[SOURCE: ISO/TS 11139:2006, definition 2.6]

根据暴露于某过程后发生的化学或物理变化，反映一个或多个预定过程变量变化的测试系统。

[ISO/TS11139：2006，定义2.6]

3.7 Conditioning 处理

treatment of product within the sterilization cycle, but prior to ethylene oxide admission, to attain a predetermined temperature and relative humidity

在加入环氧乙烷之前，对灭菌周期内的产品进行处理，以达到预定温度和相对湿度。

Note 1 to entry: This part of the sterilization cycle can be carried out either at atmospheric pressure or under vacuum.

注1，该部分灭菌周期可在大气压下或真空下进行。

Note 2 to entry: See 3.27, preconditioning 见3.27，预处理

3.8 *D* value D值

D_{10} value D_{10}值

time or dose required to achieve inactivation of 90 % of a population of the test microorganism under stated conditions

[SOURCE: ISO/TS 11139:2006, definition 2.11]

在设定条件下，灭活90%测试微生物所需的时间或辐射剂量。

Note 1 to entry: For the purposes of this International Standard, the *D* value is the exposure time required to achieve 90 % inactivation of the population of the test organism.

注：本标准中的D值是指灭活90%测试微生物所需的暴露时间。

3.9 Development 开发

act of elaborating a specification

确定某规范的行为。

[SOURCE: ISO/TS 11139:2006, definition 2.13]

3.10 dew point 露点

The temperature at which the saturation water vapour pressure is equal to the partial pressure of the water vapour in the atmosphere

大气中的水蒸汽由于温度下降，水蒸气的压力等于饱和蒸汽压而凝结时的温度

Note 1 to entry: Any cooling of the atmosphere below the dew point would produce water condensation.

任何露点以下的大气的冷却会产生水凝。

3.11 Establish 建立

determine by theoretical evaluation and confirm by experimentation

[SOURCE: ISO/TS 11139:2006, definition 2.17]

通过理论评价与试验确认进行确定。

3.12 ethylene oxide (EO) injection time 环氧乙烷注入时间

duration of the stage beginning with the first introduction of the EO (mixture) into the chamber to the completion of that injection

从环氧乙烷最初进入灭菌柜开始至环氧乙烷气体或环氧乙烷混合气体加入结束阶段的时间。

3.13 exposure time 暴露时间

period for which the process parameters are maintained within their specified tolerances

[SOURCE: ISO/TS 11139:2006, definition 2.18]

过程参数保持在规定公差内的持续时间

Note 1 to entry: For the purpose of calculation of cycle lethality, it is the period of sterilization between the end of EO injection and the beginning of EO removal.

出于周期杀伤力计算的目的，是指环氧乙烷注入时间结束至环氧乙烷去除开始之间的灭菌周期

3.14 Fault 故障

one or more of the process parameters lying outside of its/their specified tolerance(s)

[SOURCE: ISO/TS 11139:2006, definition 2.19]

一个或多个过程参数超出其规定的公差。

3.15 Flushing 换气

procedure by which the ethylene oxide is removed from the load and chamber by either multiple alternate admissions of filtered air, inert gas or steam and evacuations of the chamber or continuous passage of filtered air, inert

gas or steam through the load and chamber

通过以下方法之一去除物品或柜室内环氧乙烷的过程:

a）多次交替将经过滤的空气或惰性气体加入柜室，然后再抽空柜室内气体，或

b）不断将经过滤的空气或惰性气体通过被灭菌物品或柜室。

3.16 fractional cycle 短周期

a cycle in which the exposure time to EO gas is reduced compared to that specified in the sterilization process

与灭菌过程规定的EO作用时间相比，作用时间减少的灭菌周期。

3.17 half cycle 半周期

a cycle in which the exposure time to EO gas is reduced by 50 % compared to that specified in the sterilization process

与灭菌过程相比，EO作用时间减少50%的灭菌周期。

3.18 health care facility 医疗保健机构 HCF

governmental and private organizations and institutions devoted to the promotion and maintenance of health, and the prevention and treatment of diseases and injuries

致力于促进和维护健康，以及疾病和伤害的预防和治疗的政府和私人组织和机构

EXAMPLE A health care facility can be a hospital, nursing home, extended care facility, free-standing surgical centre, clinic, medical office, or dental office.

例：一个医疗保健机构可以是医院，疗养院，延长护理设施，独立的手术中心，诊所，医务室，或牙科办公室

3.19 health care product 医疗保健产品

medical device(s), including *in vitro* diagnostic medical device(s), or medicinal product(s), including biopharmaceutical(s)

[SOURCE: ISO/TS 11139:2006, definition 2.20]

医疗器械，包括在体外诊断试剂，或药用产品，包括生物药品

3.20 installation qualification 安装验证IQ

process of obtaining and documenting evidence that equipment has been provided and installed in accordance with its specification

[SOURCE: ISO/TS 11139:2006, definition 2.22]

证明并记录设备已按照规范提供和安装的过程。

3.21 medical device 医疗器械

any instrument, apparatus, implement, machine, appliance, implant, *in vitro* reagent or calibrator, software, material or related article, intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the specific purpose(s) of

— diagnosis, prevention, monitoring, treatment or alleviation of disease,

— diagnosis, monitoring, treatment, alleviation of, or compensation for an injury,

— investigation, replacement or modification or support of the anatomy or of a physiological process,

— control of conception,

— disinfection of medical devices,

— providing information for medical purposes by means of *in vitro* examination of specimens derived from the human body, and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means

[SOURCE: ISO 13485:2003, definition 3.7]

为以下目的应用于人体的，单独使用或联合使用的任何仪器、设备、器具、植入物、体外试剂、软件、材料或其他物品：

- 疾病的诊断、预防、监护、治疗、缓解；
- 伤残的诊断、监护、治疗、缓解或修补；
- 人体结构或生理过程的研究、替代或调节；
- 妊娠的控制；
- 医疗器械的消毒；
- 通过人体样本体外检查方式提供医疗信息

其对于人体内或人体上的主要预期作用不是用药理学、免疫学或代谢的手段获得，但可以在这些手段的应用中起辅助作用。

3.22 microorganism 微生物

entity of microscopic size, encompassing bacteria, fungi, protozoa and viruses

包括细菌、真菌、原生生物、病毒在内的个体微小的实体。

Note 1 to entry: A specific standard might not require demonstration of the effectiveness of the sterilization process in inactivating all types of microorganisms, identified in the definition above, for validation and/or routine control of the sterilization process.

[SOURCE: ISO/TS 11139:2006, definition 2.26]

注1：特定的标准可能不要求为灭菌过程确认和常规控制证实灭菌过程灭活以上定义规定的全部类型微生物的有效性。

3.23 operational qualification 操作验证OQ

process of obtaining and documenting evidence that installed equipment operates within predetermined limits when used in accordance with its operational procedures

[SOURCE: ISO/TS 11139:2006, definition 2.27]

证明并记录，按操作程序进行使用时，已安装设备能在预定范围内进行运行。

3.24 overkill approach过度杀灭方法

approach using sterilization process that delivers a minimum of 12 Spore Log Reduction (SLR) to a biological indicator having a resistance equal to or greater than the product bioburden

证明具有与产品生物负载相等或较大抗力的生物指示物孢子对数下降值(SLR)至少为12的灭菌过程的方法。

3.25 parametric release 参数放行

declaration that product is sterile, based on records demonstrating that the process parameters were delivered within specified tolerances

[SOURCE: ISO/TS 11139:2006, definition 2.29]

根据过程参数在规定公差内的记录，决定产品无菌。

Note 1 to entry: This method of process release does not include the use of biological indicators.

注：本过程放行方法不涉及使用生物指示物。

3.26 performance qualification 性能验证PQ

process of obtaining and documenting evidence that the equipment, as installed and operated in accordance with operational procedures, consistently performs in accordance with predetermined criteria and thereby yields product meeting its specification

[SOURCE: ISO/TS 11139:2006, definition 2.30]

获得并出具书面证明的过程，已安装设备按操作程序进行操作时，能持续按预定准则发挥性能并生产合格产品。

3.27 Preconditioning 预处理

treatment of product, prior to the sterilization cycle, in a room or chamber

to attain specified conditions for temperature and relative humidity

灭菌周期开始前，在一房间或柜室内先对产品进行处理，以达到预定的温度和相对湿度。

3.28 process challenge device 过程挑战器具PCD

item designed to constitute a defined resistance to a sterilization process and used to assess performance of the process

[SOURCE: ISO/TS 11139:2006, definition 2.33]

设计成对灭菌过程具有确定的抗力，用于评估过程性能的器具。

Note 1 to entry: For the purpose of this International Standard, a PCD can be product, simulated product or other device that is inoculated directly or indirectly. See 7.1.6 and D.7.1.6.

就本标准而言，PCD可以是产品、模拟产品、或直接或间接被接种的其他器具，见7.1.6和D7.1.6

Note 2 to entry: In this International Standard, a distinction is made between an internal PCD and an external PCD. An internal PCD is used to demonstrate that the required product SAL is achieved. A PCD located within the confines of the product or product shipper case is an internal PCD, whereas a PCD located between shipper cases or on the exterior surfaces of the load is an external PCD. An external PCD is an item designed to be used for microbiological monitoring of routine production cycles.

注2 本标准中有内部PCD和外部PCD之分。内部PCD被用来证明指定的产品已达到无菌保证水平。放置于产品内部或销售包装内的PCD是一个内部的PCD，而放置于产品销售包装之间或装载的外表面上的PCD是外部PCD。外部PCD只是用来日常生产过程的微生物监测。

3.29 process parameter 过程参数

specified value for a process variable

过程变量的规定值。

Note 1 to entry: The specification for a sterilization process includes the process parameters and their tolerances.

[SOURCE: ISO/TS 11139:2006, definition 2.34]

注：灭菌过程规范包括过程参数和其公差。

3.30 process variable 过程变量

condition within a sterilization process, changes in which alter microbicidal effectiveness

灭菌过程的条件，它的变化会改变微生物的效力。

EXAMPLE, Time, temperature, pressure, concentration, humidity, wavelength.

[SOURCE: ISO/TS 11139:2006, definition 2.35]

如：时间、温度、压力、密度、湿度、波长?。

3.31 processing category 加工组

collection of different product or product families that can be sterilized together

能一起灭菌的不同产品或产品族的组合

Note 1 to entry: All products within the category have been determined to present an equal or lesser challenge to the sterilization process than the process challenge device for that group.

该组合内的所有产品的灭菌过程挑战力已被确定为与该组PCD呈现相等或更低。

3.32 Product 产品

result of a process 过程的结果

[SOURCE: ISO 9000:2005, definition 3.4.2]

Note 1 to entry: For the purposes of sterilization standards, product is

tangible and can be raw material(s), intermediate(s), sub-assembly(ies) and health care products.

注：本标准所说的产品是指实物，可以是原材料、媒介、集合或医疗保健产品。

3.33 product family 产品族

group of product possessing characteristics that allow them to be sterilized using defined process conditions

可以用规定的过程条件灭菌的，类似加工特性的产品系列。

3.34 product load volume产品装载容积

defined space within the usable chamber volume occupied by product

产品在灭菌柜中占用的规定的空间。

3.35 recognized culture collection 认可的培养物存储机构

depository authority under the Budapest Treaty on *The International Recognition of the Deposit of*

Microorganisms for the Purposes of Patent and Regulation

[SOURCE: ISO/TS 11139:2006, definition 2.38]

3.36 reference microorganism 基准微生物

microbial strain obtained from a recognized culture collection

从认可的培养物存储机构获得的微生物菌种

3.37 Requalification 重新验证

repetition of part of validation for the purpose of confirming the continued acceptability of a specified process

为证实规定过程持续认可而进行的部分确认的重复；

3.38 reusable medical device 可重复使用医疗器械

medical device designated or intended by the manufacturer as suitable for

reprocessing and re-use

制造商设计或规定的作为适合于重新加工或重复使用的医疗器械

Note 1 to entry: This is not a medical device that is designated or intended by the manufacturer for single use only.

注，并不是指制造商设计或规定的一次性使用的医疗器械

3.39 Services 服务

supplies from an external source, needed for the correct function of equipment

EXAMPLE Electricity, water, compressed air, drainage.

[SOURCE: ISO/TS 11139:2006, definition 2.41]

3.40 single use medical device 一次性使用医疗器械

medical device designated or intended by the manufacturer for one-time use only

3.41 Specify 规定

stipulate in detail within an approved document

在批准的文件内详细指定

3.42 Spore-log-reduction 孢子对数下降值SLR

log of initial spore population, N_0, minus the log of the final population, N_u

描述生物指示物在暴露于规定条件下后孢子数下降值的系数，该系数为10的对数。

[SOURCE: ISO 14161:2009, definition 3.19]

Note 1 to entry: Describing the reduction in the number of spores on a biological indicator or inoculated item produced by exposure to specified conditions.

SLR计算方式为生物指示物的初始孢子数的对数减最终孢子数的对数。

For Direct Enumeration公式:

SLR = log N_0 – log N_u

where

N_0 is the initial population初始数;

N_u is the final population最终数.

For Fraction Negative:

SLR = log N_0 – log [ln (q/n)]

where

N_0 is the initial population;

q is the number of replicate samples tested;

n is the number of samples negative for growth.

If there are no survivors, the true SLR cannot be calculated. The SLR can be reported as “greater than” log N_0 if one surviving organism is used.

如没有存活微生物，则无法计算实际SLR。如果一个微生物呈阳性或存活，则SLR表述为“大于”$\log N_0$。

3.43 Sterile 无菌

free from viable microorganisms 无存活微生物

[SOURCE: ISO/TS 11139:2006, definition 2.43]

3.44 sterile barrier system无菌屏障系统

minimum package that prevents ingress of microorganisms and allows aseptic presentation of the product at the point of use

[SOURCE: ISO/TS 11139:2006, definition 2.44]

3.45 Sterility 无菌状态

state of being free from viable microorganisms 保持无存活微生物的一种状态

Note 1 to entry: In practice, no such absolute statement regarding the absence of microorganisms can be proven.

实际上，不存在此类绝对的声明，证明微生物存在与否。

Note 2 to entry: See 3.47, sterilization.

[SOURCE: ISO/TS 11139:2006, definition 2.45]

3.46 sterility assurance level 无菌保证水平SAL

probability of a single viable microorganism occurring on an item after sterilization

灭菌后，在单位产品上检出存活微生物的概率。

Note 1 to entry: The term SAL takes a quantitative value, generally 10^{-6} or 10^{-3}. When applying this quantitative value to assurance of sterility, an SAL of 10^{-6} has a lower value but provides a greater assurance of sterility than an SAL of 10^{-3}.

注：SAL为定量值，通常为10^{-6}或10^{-3}。将此定量值用于无菌保证时，10^{-6}SAL数值比10^{-3}SAL小，但高于10^{-3}SAL的无菌保证。

[SOURCE: ISO/TS 11139:2006, definition 2.46]

3.47 Sterilization 灭菌

validated process used to render product free from viable microorganisms

已确认的使产品无存活微生物的过程。

Note 1 to entry: In a sterilization process, the nature of microbial inactivation is exponential and thus the survival of a microorganism on an individual item can be expressed in terms of probability. While this probability can be reduced to a very low number, it can never be reduced to zero.

注：灭菌过程中，微生物的死亡规律用指数函数表示，因此，任何单件产品上微生物的存在可用概率表示。概率可减少到最低，但不可能到零。

Note 2 to entry: See 3.46, sterility assurance level.

[SOURCE: ISO/TS 11139:2006, definition 2.47]

3.48 sterilization cycle 灭菌周期

treatment in a sealed chamber, which includes air removal, conditioning (if used), injection of ethylene oxide, inert gas (if used), exposure to ethylene oxide, removal of ethylene oxide and flushing (if used), and air/inert gas admission

在一密闭的柜室内，包括进行去除空气、处理（若采用）、加入EO、EO作用、去除EO和换气（若采用）、及加入空气/惰性气体的一系列处理的步骤。

3.49 sterilization load 被灭菌产品（灭菌装载）

product to be, or that has been, sterilized together using a given sterilization process

用同一灭菌过程一起灭菌或已灭菌的产品

[SOURCE: ISO/TS 11139:2006, definition 2.48]

3.50 sterilization process 灭菌过程

series of actions or operations needed to achieve the specified requirements for sterility

[SOURCE: ISO/TS 11139:2006, definition 2.49]

为达到规定无菌要求所需的一系列动作或操作。

Note 1 to entry: This series of actions or operations includes preconditioning (if necessary), exposure to the ethylene oxide under defined conditions and any necessary post-treatment required for the removal of ethylene oxide and its by-products. It does not include any cleaning, disinfection or packaging operations that precede the sterilization process.

注：这一系列动作或操作包括预处理（若采用）、在规定条件下暴露于EO和任何去除EO及其产物所需的后处理。但不包括灭菌过程之前的任何清洗、消毒或包装操作。

3.51 sterilization specialist 灭菌专家

person with technical knowledge of the sterilization technology being utilized and its effects upon materials and microorganisms

3.52 sterilizing agent 灭菌剂

physical or chemical entity, or combination of entities having sufficient microbicidal activity to achieve sterility under defined conditions

具有充分杀死微生物能力的在规定条件下能够达到无菌的物理或化学物质或物质组合。

[SOURCE: ISO/TS 11139:2006, definition 2.50]

3.53 survivor curve 存活曲线

graphical representation of the inactivation of a population of microorganisms with increasing exposure to a microbicidal agent under stated conditions

[SOURCE: ISO/TS 11139:2006, definition 2.51]

在规定条件下，微生物灭活与暴露于微生物杀灭剂的时间之间的图状说明。

3.54 test for sterility 无菌试验

technical operation defined in a Pharmacopoeia performed on product following exposure to a sterilization process

[SOURCE: ISO/TS 11139:2006, definition 2.53]

3.55 test of sterility 无菌检查

technical operation performed as part of development, validation, or requalification to determine the presence or absence of viable microorganisms on product or portions thereof

开发、确认或重新确认的一部分，确定产品上是否存在存活微生物的技术操作。

[SOURCE: ISO/TS 11139:2006, definition 2.54]

3.56 usable chamber volume 柜室可用体积

defined space within the sterilizer chamber, which is not restricted by fixed or mobile parts and which is available to accept the sterilization load

灭菌器柜室内不受固定或可移动部件限制的，可容纳被灭菌物品的空间。

Note 1 to entry: The volume allowed for gas circulation around the load inside the chamber is not included as usable space.

注：用于循环的空间不计算在可用空间内

3.57 Validation 确认

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

[SOURCE: ISO/TS 11139:2006, definition 2.55]

对获得的结果进行整理和记录的书面程序，证明某过程可持续生产符合预定规格的产品。

3.58 virgin material 新材料

material that has not been previously used, or subjected to processing other than for its original production

没被使用过的或被

4 Quality management systems 质量管理体系

4.1 Documentation 文件

4.1.1 Procedures for development, validation, routine control and product release from sterilization shall be specified.

应规定灭菌开发、确认、常规控制和产品放行的程序。

4.1.2 Documents and records required by this International Standard shall be reviewed and approved by designated personnel (see 4.2.1). Documents and

records shall be controlled in accordance with the applicable clauses of ISO 13485.

本标准所要求的文件和记录应由指定人员进行审核和批准（见4.2.1）。文件和记录应按照ISO13485的适用条款进行控制。

4.2 Management responsibility 管理职责

4.2.1 The responsibility and authority for implementing and meeting the requirements described in this International Standard shall be specified. Responsibility shall be assigned to competent personnel in accordance with the applicable clauses of ISO 13485.

应规定实施和满足本标准要求的职责和权限。职责应按ISO13485的适用条款分配给能胜任的人员。

D.4.2.1 Requirements for responsibility and authority are specified in ISO 13485:2003, 5.5, and requirements for human resources are specified in ISO 13485:2003, 6.2.

ISO13485：2003中的5.5条款规定了职责和权限的要求，6.2条款规定了人力资源的要求。

In ISO 13485, the requirements for management responsibility relate to management commitment, customer focus, quality policy, planning, responsibility, authority and communication, and management review.

ISO13485的管理职责涉及到管理承诺，顾客焦点，质量方针，策划，职责、权限与沟通，及管理评审。

Each organization should establish procedures for identifying training needs and ensure that all personnel are trained to adequately perform their assigned responsibilities.

每个机构应建立规定培训要求的程序，以确保所有人员都能胜任他们的职责。

4.2.2 If the requirements of this international standard are undertaken by organizations with separate quality management systems, the responsibilities and authority of each party shall be specified.

如果本标准的要求由具有独立质量管理体系的机构承担，则各方的职责和权限应加以规定。

When a HCF contracts out the sterilization of reusable medical devices, it is the HCF’s responsibility for validation and release of the sterilized product.

当医疗保健机构将可重复使用医疗器械的灭菌外包时，灭菌产品的确认和放行是医疗保健机构的职责。

D.4.2.2 The development, validation and routine control of a sterilization process can involve a number of separate parties, each of whom is responsible for certain elements. It is important that the respective procedures clearly outline the responsibilities for meeting the requirements of this International Standard. This is especially important where contractors are engaged to carry out specific functions.

灭菌过程的开发、确认和日常控制能分成许多独立的环节，每个环节对某些要素负责。为满足本标准的要求，各自职责明确的流程是十分重要的；如果由承包商来完成某些项目，这尤其重要。

Even where elements of the sterilization process are contracted out it is important to note that the medical device manufacturer is ultimately responsible for validation, release and distribution of sterilized product to the market. When a health care facility contracts out the sterilization of reusable medical devices, it is the health care facility’s responsibility for validation and release of the sterilized product

无论灭菌过程的哪个要素被分包，应注意，确认、灭菌产品的放行和分发到市场仍是医疗器械制造商的职责。当医疗机构将可重复使用医疗器械的灭菌过程外包时，灭菌产品的确认和放行是医疗机构的职责。

Further guidance is available in ISO 14937:2009, E.4.2.2.

4.3 Product realization 产品实现

D.4.3 NOTE In ISO 13485, the requirements for product realization relate to the product lifecycle from the determination of customer requirements, design and development, purchasing, control of production, and calibration of monitoring and measuring devices.

产品实现的要求涉及到产品生命周期，产品生命周期取决于顾客要求、设计开发、采购、过程控制和监视和测量器械的校验。

4.3.1 Procedures for purchasing shall be specified. These procedures shall comply with the applicable clauses of ISO 13485.

应规定采购程序。这些程序应符合ISO13485适用条款的要求。

D.4.3.1 Requirements for purchasing are specified in ISO 13485:2003, 7.4. In particular, it should be noted that the requirements in ISO 13485:2003, 7.4 for verification of purchased product apply to product and services, that impact on process quality, received from outside the organization.

ISO13485：2003中的7.4条款规定了采购的要求。特别要注意，ISO13485：2003中的7.4条款的针对应用于产品和服务的、影响过程质量的、来自外部机构的采购产品的验证的要求。

Purchasing procedures in a health care facility should ensure that reusable medical devices are supplied with validated instructions for cleaning, disinfection, sterilization and aeration as specified in ISO 17664. It should also be verified that the prescribed procedure for cleaning, disinfection, sterilization and aeration can be performed in the health care facility.

根据ISO17444的要求，医疗机构的采购程序应确保重复使用医疗器械按已验证的清洗、消毒、灭菌和通风的规范要求来供应。应证明医疗机构实施了规定的清洗、消毒、灭菌和通风的流程。

4.3.2 Procedures for identification and traceability of product shall be specified. These procedures shall comply with the applicable clauses of ISO 13485.

应规定产品标识和可追溯性程序。这些程序应符合ISO13485适用条款的要求。

D.4.3.2 Requirements for identification and traceability are specified in ISO 13485:2003, 7.5.3.

在ISO13485：2003的7.5.3中规定了标识和可追溯性的要求；

For those facilities that do not fully comply with ISO 13485, such as health care facilities, procedures for identification of product and maintenance of traceability should include the labelling of each item or package prior to sterilization with a lot control identifier that includes the following information:

对那些并不完全符合 ISO 13485的机构，如医疗机构， 其产品标识和可追溯性程序应包括灭菌前的每一单件或每一包装件的批控制标识，并包括下列信息:

a) the sterilizer ID or code;灭菌器的ID或代码；

b) the date of sterilization;灭菌日期

c) the cycle number (i.e. the cycle run of the day or sterilizer);

周期编号(如，当天的或灭菌柜的运行序号)

d) the identity of the person who assembled the pack.

操作人的身份

Including the identity of the person who assembled the pack allows for further investigation if a problem should arise. Lot identification information enables personnel to retrieve items sterilized in a specific cycle in the event of a recall and to trace problems to their source.

如出现问题时，可以调查到更详细的操作人的身份。批标识信息可以使人员在召回事件中更容易取回问题灭菌产品，以及追溯问题的根源。

4.3.3 A system complying with the applicable clause(s) of ISO 13485 or ISO 10012 shall be specified for the calibration of all equipment, including instrumentation for test purposes, used in meeting the requirements of this

International Standard.

应规定所有设备(包括用于满足本标准要求的测试仪器)校准的体系，体系应符合ISO13485或ISO10012适用条款的要求。

D.4.3.3 Requirements for calibration of monitoring and measuring instrumentation are specified in ISO 13485:2003, 7.6.

ISO 13485:2003中的7.6条规定了监视和测量装置的校验要求。

4.4 Measurement, analysis and improvement — Control of nonconforming product
测量、分析和改进——不合格产品的控制

Procedures for control of product designated as nonconforming and for correction, corrective action and preventive action shall be specified. These procedures shall comply with the applicable clauses of ISO 13485.

应规定被判定为不合格品的控制程序，及其纠正、纠正措施和预防措施的程序。这些程序应符合ISO13485适用条款的要求。

D.4.4 Procedures for control of non-conforming product and corrective action are specified in ISO 13485:2003, 8.3 and 8.5.2, respectively.

ISO 13485:2003中的8.3 和8.5.2条分别规定了不合格品的控制和纠正措施的要求。

5 Sterilizing agent characterization 灭菌剂特性

5.1 General通则

The purpose of this activity is to define the sterilizing agent, demonstrate its microbicidal effectiveness, identify the factors that influence microbicidal effectiveness, assess the effects that exposure to the sterilizing agent has on materials, and identify requirements for safety of personnel and protection of the environment. This activity may be undertaken in a test or prototype system. Where this occurs, the final equipment specification (see 6.3) shall be relatable to the results of experimental studies undertaken in the test or prototype equipment. For the purposes of this International Standard, the sterilizing agent is EO.

本章节是为了定义灭菌剂，指明它的灭菌效果，识别影响灭菌效果的因素，评价灭菌剂对材料的影响，识别人员安全和环境防护的要求。这些活动可以由试验或样机系统来承担。无论在哪里进行，最终设备规范(见6.3)应与试验或样机设备的研究结果一致。本标准所指的灭菌剂是EO.

5.2 Sterilizing agent 灭菌剂

The sterilizing agent specification shall include, if appropriate, conditions of storage to maintain the EO within its specification for the duration of the stated shelf life.

如果适用，灭菌剂规范应当包括，为保证声称的保质期所规定的EO储存条件。

D.5.2 EO is a highly penetrative gas that will permeate most packaging materials and polymeric materials. Widely recognized compositions include pure EO and mixtures with carbon dioxide or nitrogen.

EO 是高穿透性气体，可穿透绝大多数包装材料和聚合材料。广泛认同的成份包括纯EO和EO与二氧化碳或氮气的混合物。

NOTE, For EO gas mixtures with carbon dioxide, nitrogen or other inert gas blends, EO molecular diffusion rates into polymer materials can be affected by the volume percent of EO gas molecules within the sterilant, which can result in longer EO exposure times to achieve the desired microbiological spore log reduction.

与二氧化碳、氮气或其他惰性气体混合的EO混合物，EO分子进入聚合材料的扩散速率可能会受灭菌剂中EO分子体积百分比的影响，这样可能导致达到规定的微生物孢子对数下降需更长EO暴露时间。

The storage conditions and shelf life for EO should be in accordance with the EO manufacturer’s recommendations and all applicable regulations. This is particularly important with premixed gas mixtures where stratification might be an issue.

EO 的储存条件和有效期应符合 EO生产商的建议和所有适用的规定。不管是否产生分

层，混合气体的预先混合尤其重要。

5.3 Microbicidal effectiveness 杀灭微生物效果

Microbicidal effectiveness data shall be developed if it is proposed to use the EO outside of the range of compositions that are widely recognized or if a novel diluent is to be used.

如果使用的环氧乙烷超出公认的成分范围或使用新的稀释物，则应开发杀灭微生物的有效性数据。

NOTE The inactivation of microorganisms by EO has been comprehensively documented in literature. This literature provides knowledge of the manner in which the process variables affect microbial inactivation. Reference to these general studies on microbial inactivation is not required by this International Standard.

注：环氧乙烷对微生物的灭活性能已在文献中作全面记录，这个知识提供了过程变量影响微生物灭活的手段。本标准未对有关这些微生物灭活的普遍性研究作出要求。

5.4 Material effects材料影响

The effects of EO on a wide variety of materials used to manufacture medical devices have been comprehensively documented and such documentation is of value to those designing and developing medical devices that are to be sterilized by EO. This International Standard does not require the performance of specific studies on material effects, but does require performance of studies of the effects of EO on product (see Clause 7).

环氧乙烷对用于医疗器械制造的一系列材料的影响已得到全面记录，这些记录对使用环氧乙烷灭菌的医疗器械设计和开发具有一定价值。本标准不要求进行对具体材料影响的研究，但要求进行EO对产品影响的研究（见第7条）。

5.5 Safety and the environment安全和环境

5.5.1 Either a material safety data sheet (MSDS) or analogous safety information shall be made available for EO and its diluents (if any). Measures

necessary to protect the health and safety of personnel shall be identified.

EO及其稀释剂应有材料安全清单(MSDS)或类似的安全报告。应规定人员安全和健康保护的必要措施。

D.5.5.1 EO is toxic, flammable and explosive; therefore, extreme caution should be used during its handling and use. The explosive limits are 2,6 % to 100 % EO by volume in air.

EO是有毒、易燃、易爆物质，因此，在使用时要格外的小心。其爆炸极限是空气中含有2.6%～100%的EO。

Where practical, EO sterilization cycles should operate within the non-flammable region throughout the complete sterilization cycle in order to minimize the risk of explosion. This requires the removal of air from the chamber prior to the introduction of EO gas. For 100 % EO sterilization processes this can be achieved by pulling a deep vacuum or by pulling several partial vacuums, each of which is followed by injection of an inert gas, e.g. nitrogen. This purges air from the chamber allowing EO gas to be injected into the chamber in a safe manner. On completion of the EO gas exposure phase it is necessary to remove the EO gas from the chamber until the level of gas is below the 2,6 % explosive limit. This is achieved by pulling several post-vacuums, each of which is followed by a nitrogen backfill.

不管怎样，为了使爆炸风险最小化，整个灭菌周期应在不易燃烧的区域内运行。这要求在EO导入前将灭菌柜室内的空气去除。对于使用100%EO的灭菌过程，可以通过抽深度真空或部分真空的方法来达到，不管哪个方法都可以用注入惰性气体如氮气的方法来排除空气。这样将柜室内的空气去除，使得EO安全地注入柜室。当EO暴露阶段结束时，必须将灭菌柜室内的EO气体浓度抽至2.6%的爆炸极限以下。可以通过多抽几次过真空然后回填氮气来完成。

The use of non-flammable sterilant blends can improve safety by decreasing the risk of fire or explosion. They can also facilitate compliance with country-specific equipment safety requirements. Nonflammable blends are

produced by mixing the highly flammable EO gas with one or more inert gases. The flammability of such a mixture can be assessed by measuring the relative proportions of EO, air, diluent gas (e.g. CO_2, etc.), inert gas (e.g. nitrogen) and water vapour in the sterilizer. Caution should be exercised to ensure no separation of the EO blend can occur as this might lead to safety and quality issues.

使用非可燃性混合灭菌剂，降低着火或爆炸的风险来提高安全性。这也容易符合国家特种设备安全要求。非可燃性混合灭菌剂由高可燃性EO气体与一种或多种惰性气体混合而成。这种混合气体的可燃性可以通过测定灭菌柜室内的EO、空气、稀释气体(如二氧化碳等)、惰性气体(如氮气)和水蒸汽的比例来评估。应注意，混合气体的分层可能导致安全和质量事故。

Ethylene oxide sterilizers should be installed in a dedicated room. The operating controls for the sterilization equipment should be mounted outside the room so that operators can set or change program parameters without entering the sterilization room. All airflow from the sterilizer access area should be exhausted to the outdoors and comply with applicable requirements.

环氧乙烷灭菌柜应安装在专用房间内。灭菌柜的操作控制应安装在灭菌柜房间外，使操作者在不进入灭菌间就可以设定或调整项目参数。用适当的设备，将来自灭菌柜区域的全部空气排出户外。

Prior to removing product from a sterilizer, precautions should be taken to ensure that operators are not exposed to levels of EO above relevant worker exposure limits [permissible exposure limit (PEL)/short term exposure limit STEL)] due to the outgassing of the load. When products sterilized with inert EOgas mixtures are not immediately removed from the sterilizer at the end of a cycle the EO concentrations in the sterilizer might result in personnel safety issues.

在将产品移出灭菌柜前，应采取预防措施，以确保操作员工不会处于由于产品解析EO而超过安全极限的环境里。如果用混合气体灭菌，当周期结束后，未马上将产品从灭菌柜内移出时，灭菌柜内的EO浓度可能导致人员安全事故。

5.5.2 The potential effect on the environment of the operation of the sterilization process shall be assessed and measures to protect the environment shall be identified. This assessment, including potential impact and measures for control, shall be documented.

应评估灭菌过程对环境的潜在影响，并规定保护环境的措施。应记录所进行的评估，包括潜在危害和控制措施。

D.5.5.2 Principles of an environmental management system can be applied to the EO sterilization process. ISO 14001 provides a specification for an environmental management system. ISO 14040 provides guidance on designing a life cycle assessment study.

环境管理体系的原则可以应用于EO灭菌过程。ISO14001提供了环境管理体系的规定。ISO14040提供了关于生设计命周期评估研究的指南。

5.5.3 Users of EO shall comply with applicable local, national and international requirements regarding the emission and disposal of EO and its diluents as well as any by-products.

对于EO和稀释剂及其副产物的排放和处理，EO使用者应符合适当的地区、国家和国际的要求。

D.5.5.3 Effluent gas should be discharged through an EO gas treatment system, such as a catalytic oxidizer, wet acid scrubber or thermal oxidizer in compliance with local permit requirements or emission control legislation.

废气应通过一个EO气体处理系统排放，如，符合当地许可要求或排放控制法规的催化氧化器，湿酸洗涤器或热氧化器。

When choosing a diluent, the ozone depleting potential of the diluent as well as the disposal of any byproducts should be taken into consideration.

选择稀释剂时，应考虑稀释剂及其副产物的臭氧消耗潜力。

6 Process and equipment characterization 过程和设备特征

D.6 In health care facilities, process and equipment characterization are

generally the responsibility of the sterilizer manufacturer. The management of the health care facility should have controls in place to ensure that the equipment it purchases conforms to national, regional and local regulations and is suitable for use to sterilize products that require EO sterilization. The management of the health care facility should ensure that the facility has the infrastructure necessary to correctly operate the sterilizing equipment and to achieve effective sterilization of medical devices.

在医疗机构，过程和设备特征通常是制造商的职责。医疗机构的管理应控制到位，以确保采购的设备符合国家、地区和地方法规的要求，并适用于产品的EO灭菌过程。医疗机构的管理应确保机构具有必要的基础设施，以完成灭菌设备的正确操作，并能达到有效的医疗器械灭菌过程。

6.1 General 通则

6.1.1 The purpose of this activity is to define the entire sterilization process and the equipment necessary to deliver the sterilization process safely and reproducibly.

这一活动的目的是定义整个灭菌过程及可提供安全和可重复灭菌过程所必需的设备。

6.1.2 If an existing process has been used to sterilize product this activity is not required, however, the process and equipment should be reviewed to ensure the identified variables in 6.2 and 6.3 have been included in the process specification for routine production.

如果目前的过程已被用于灭菌产品，这一活动不是必需的，然而，应对灭菌过程和设备进行评审，以确保在6.2和6.3所定义的变量已包含在日常生产的过程规范中。

6.2 Process characterization过程特征

6.2.1 Process characterization, at a minimum, shall include:

过程特征，至少应包含：

a) identifying the phases that are necessary for an EO sterilization process;

识别EO灭菌过程所必需的阶段；

b) identifying the process variables for each phase;

识别每个阶段的过程变量

c) documenting the process variables.

记录过程变量

NOTE The data developed in product definition (see Clause 7) can impact the characterization of the sterilization process.

注，在产品定义(见7)时开发的数据可能影响灭菌过程特征

6.2.2 The phases of the sterilization process include:

灭菌过程的阶段包括:

a) preconditioning (if used);预处理(如采用)

b) the sterilization cycle;灭菌周期

c) aeration (if used).通风(若采用)

D.6.2.2 The resistance of microorganisms to deactivation by EO is affected by their moisture content. At low levels of humidity, below 30 %, microbial resistance may increase with decreased humidity for some products. For this reason it is common practice to control and monitor the humidity of the atmosphere to which the product is exposed in order to attempt to equilibrate the moisture content of the microorganisms with the local conditions. Consideration should be given to the packaged product to ensure that excessive relative humidity will not impact the product functionality and package integrity. One of the ways to assist in addressing the humidity in the product is to precondition product at a defined temperature and humidity. Such preconditioning can reduce the duration of the sterilization cycle. For health care facilities, excessive moisture content can also be caused by inadequate drying after cleaning.

微生物对EO的抵抗力受他们的水分含量的影响。在较低的湿度水平下，低于30%,有些

产品微生物的抵抗力会增加。由于上述原因,通常测定和控制与产品接触的空气湿度,促使微生物的水分含量与当地条件一致;应考虑到过高的相对湿度对已包装产品的产品性能和产品包装完整性的影响。帮助提高产品湿度的方法之一是在规定的温度和湿度下预处理产品。这样的预处理能减少灭菌周期的时间。对医疗机构而言,清洗后未充分干燥可能引起过高的水分含量。

Product heating and humidification are used to establish reproducible product temperature and moisture content prior to EO exposure. Studies establishing minimum residence time in preconditioning cells/rooms ensure that the required conditions are attained in the sterilization load. Precautions should be taken to prevent excessive water condensation on the sterilization load.

产品的加热和加湿可以使EO暴露前的产品的温度和水分含量达到规定的范围内。在预处理室/房的最短滞留时间确保灭菌产品内达到规定的条件。应注意灭菌产品内水的凝结。

Although it is common practice to perform preconditioning in a separate chamber, room or cell, sterilization cycles can be designed to attain the required temperature and humidity ranges within the load during a conditioning phase in the sterilization chamber. To minimize the risk of excessive condensation, it is recommended that the load temperature should be maintained above the process environmental dewpoint temperature during the preconditioning and conditioning phases of the sterilization process.

尽管在专用的柜、房间或室内进行预处理十分普遍,但也可在灭菌柜内,在处理过程期间,使灭菌产品内的温度和湿度达到规定的范围内。为降低水凝结的风险,在灭菌过程的预处理和处理阶段,将产品(装载)的温度保持在加工环境的露点温度之上。

The actual temperature and humidity ranges within the sterilization load at the end of preconditioning should be demonstrated during PQ.

PQ时应证明预处理结束时灭菌产品(装载)内的实际温度和湿度范围。

Where applicable, a maximum time between removal of the load from preconditioning and the start of the sterilization cycle needs to be

established. A transfer time of 60 min or less is common practice.

在适用情况下，应规定产品(装载)从预处理移出到灭菌周期开始的最大时间。

一般情况下，转移时间不超过60分钟。

a) When product enters the sterilization chamber without preconditioning, consideration should be given to the possibility of excessive condensation in product and packaging.

当产品未经预处理进入灭菌柜时，要考虑产品和包装中水凝结的可能性。

b) Residues of EO and its reaction products can be hazardous. It is essential for the manufacturer of the product to be sterilized to be aware of the possible occurrence of residues in the product. Temperature, dwell time, forced heated air circulation, load characteristics, product and packaging materials all affect the efficiency of aeration, and the set points and tolerances should be taken into account when evaluating residual levels as outlined in ISO 10993-7. Aeration can be performed within the sterilizer, in a separate area(s), or in a combination of both. For health care facilities it is usual to perform aeration in a chamber rather than in a room due to the hazards of exposure to EO. In health care facilities, reprocessed items sterilized with EO need to be thoroughly aerated prior to handling or use, according to the medical device and the rigid sterilizer container manufacturer's recommendations. Inadequately aerated items and packaging will release EO, which can injure patients and health care facility personnel.

EO及其产物的残留可能是有危害的。就灭菌产品的制造商而言，应关注产品内产生残留的可能性。温度、时间、强热风循环、装载特征、产品及其包装材料都可能影响通风的效果。当按ISO10993-7的要求评估残留水平时，应先设定残留物的值及其公差。通风可以在灭菌柜室内或专门的区域内进行，或二者相结合。医疗机构通常在灭菌柜内通风。在医疗机构，用EO灭菌的再加工物品在处理和使用前，应根据医疗器械和灭菌柜室的制造商的建议，对产品进行彻底的通风。通风不足的物品或包装可能释放EO，而导致病人和操作人员的伤害。

6.2.3 The process variables for preconditioning (if used) include at a minimum:

预处理(若采用)的过程变量至少应包含:

a) time;时间

b) temperature;温度

c) humidity;湿度

d) transfer time.转移时间

D.6.2.3 Transfer time refers to each transfer step during preconditioning and final transfer of product into the sterilizer to the start of cycle.

转移时间参考预处理期间的每一转移步骤和产品最后进入灭菌柜周期开始的转移。

6.2.4 The process variables for the sterilization cycle include:

灭菌周期的过程变量包含:

a) exposure time; 暴露时间

b) temperature;温度

c) humidity;湿度

d) EO concentration;EO浓度

e) pressure.压力

D.6.2.4 The following is a list of phases that can be included in a sterilization cycle along with the performance factors that might be considered for each phase:

下列是灭菌周期是可能需考虑的每个阶段的性能因素的清单:

a) air removal:空气去除

1) depth (ΔP or terminal pressure) and rate (ΔP/time) of attainment of vacuum;

真空深度(Δ*P*或终端压力)和抽真空的速率(Δ*P*/时间)

b) chamber leak test (performed either under vacuum for subatmospheric cycles or under vacuum and at pressure for superatmospheric cycles), if applicable:

柜室泄漏试验(低于大气压或真空状态下和在高于大气压状态下二都之一),如适当:

1) stabilization period and/or hold time;稳定期限和/或保持时间

2) pressure change;压力变化;

c) inert gas addition (if used);惰性气体的加入(若采用)

1) pressure (Δ*P* or terminal pressure) and rate (Δ*P*/time) of attainment of pressure on admission of the inert gas.

压力(Δ*P*或终端压力)和惰性气体进入的压力变化速率(Δ*P*/time)。

d) conditioning (if used);处理(若使用)

1) during the conditioning phase, pressure rise (Δ*P* or terminal pressure) or % relative humidity and rate (Δ*P*/time) of attainment of pressure on injection of steam;

处理阶段，压力上升或相对湿度，以及蒸汽注入时压力变化速率(Δ*P*/time)。

2) number of steam pulse/vacuum stages, if applicable;

蒸汽加入和抽出的次数，如适用;

e) EO injection:EO注入

1) pressure, pressure rise (ΔP) and rate (Δ*P*/time) of attainment of specified pressure on admission of EO and correlation of methods used to monitor EO concentration;

压力，压力上升，和注入EO时规定的压力速率(Δ*P*/time)，以及监测EO浓度的方法

2) pressure, pressure rise (ΔP) and rate (Δ*P*/time) of attainment of specified pressure on admission of any inert gasses (if used);

压力，压力上升，和注入惰性气体的规定的压力速率(Δ*P*/time)

f) maintenance of specified conditions for the exposure time:

EO暴露时间的规定条件的保持

1) pressure differential used to apply sterilant or inert gas make-ups (if used);用灭菌剂或惰性气体补偿(若采用)的压力变化。

2) chamber temperature;柜室温度

g) EO removal:EO去除

1) depth (ΔP or terminal pressure) and rate (Δ*P*/time) of attainment of vacuum to remove EO;EO去除时的压力和压力变化速率

h) flushing (if used):清洗

1) pressure rise and rate of attainment of pressure;压力上升和压力变化速率。

2) depth (ΔP or terminal pressure) and rate (Δ*P*/time) of attainment of vacuum to remove EO;去除EO的真空深度和真空速率

3) number of times of repetition and any variations in successive repetitions;重复次数和连续重复时的任何变化。

i) air/inert gas admission:空气或惰性气体的进入。

1) pressure (Δ*P* or terminal pressure) and rate (Δ*P*/time) of attainment of pressure on admission of the inert gas or air;

压力和进入惰性气体或空气的压力变化速率

2) number of times of repetition and any variations in successive repetitions;

重复次数和连续重复时的任何变化。

3) equilibration to atmospheric pressure using air admission.

使用空气与大气压平衡。

6.2.5 The process variables for aeration (if used) include at a minimum:

通风(若采用)的过程变量至少包含:

a) time;时间

b) temperature.温度

NOTE In aeration these parameters are considered process variables only if aeration is considered to contribute to ensuring the microbicidal effectiveness of the sterilization process (See AAMI TIR16:2009, clause 5.1.3.3)

如果通风只是用于协助确保灭菌过程杀灭微生物效果，通风时上述参数应是过程变量。

D.6.2.5 Recirculation velocity should be specified when assessing product residual levels.

当评估产品残留量水平时，应规定空气循环速度。

6.3 Equipment characterization 设备特征

6.3.1 The specification for the equipment to be used shall be developed and documented. This specification shall include:

应开发和记录所用设备的规范。规范应包含：

a) the preconditioning area (if used);预处理区域(若采用)

b) the sterilizer;灭菌器

c) the aeration area (if used).通风区域(若采用)

NOTE Some aspects of the equipment design may be influenced by national or regional regulatory requirements or standards.

注：一些设备设计因素可能受国家或地区法规要求和标准的影响。

D.6.3.1 The following factors should be considered when characterizing the equipment:

当表征设备时应考虑下列因素:

a) Preconditioning area characterization.预处理区的特征

Preconditioning can be performed in a separate preconditioning area (chamber, cell or room). Humidification by steam is necessary because humidifiers that operate by dispersion of unheated water as an aerosol (e.g. spinning disc humidifiers and nebulizers) can be a potential source of microbial contamination.

预处理可以在专门的预处理区（柜室，室或房间）进行。应使用蒸汽来加湿，如使用加湿器(被分散的水未经加热处理,如旋转盘加湿器和雾化器）来加湿，可能导致微生物的污染潜。

The preconditioning area (if used) should have the following performance and monitoring capabilities:

预处理区(若采用)应有下列性能和监视能力:

— adequate air circulation to ensure the uniformity of temperature and humidity in the usable space, and to ensure that uniformity is maintained in a loaded room or chamber;

  充足的空气循环，以确保可用空间的温度和湿度的均匀性，并确保在装载间或柜室内保持均匀性。

— airflow detection equipment, alarm systems or indicators monitoring the circulation system to ensure conformance to predetermined tolerances;

  测试空气流动的设备，警报系统或监视循环系统的指示，以确保规定公差的一致性。

— means of recording time of load entry into and removal from the preconditioning area;

  装载进入和移出预处理区的记录时间的手段。

— means of monitoring cell/room temperature and humidity;

监视室/房间的温度和湿度的手段

— means of controlling cell/room temperature and humidity.

控制室/房间的温度和湿度的手段

b) Sterilizer characterization.灭菌柜特征

The sterilization chamber should have the following performance and monitoring capabilities:

灭菌柜应具备下列性能和监视能力:

— means of monitoring time, chamber pressure, temperature and humidity (if humidity additions are controlled by sensor readings);

监视时间、柜室压力、温度和湿度的手段(如果加湿是靠传感器读数控制的);

— means of controlling time, chamber pressure, temperature and humidity, if humidity additions are controlled by sensor readings (when sensors are fixed on the equipment, ensure that a correlation is made during IQ or OQ to the pressure rise);

控制柜室压力、温度和湿度的手段，如果加湿是靠传感器读数控制的;[如果传感器是装在设备上的，要确保在安装鉴定或操作鉴定时压力上升具有关联性];

— if humidity is not controlled by sensor readings, means to monitor and control steam additions;

如果湿度不是由传感器读数控制的，监视和控制蒸汽加入的手段。

— if parametric release is used, analytical instrumentation for the direct analysis of humidity during conditioning and EO concentration during EO exposure time (also see 9.5.5 and D.9.5.5);

如果采用参数放行，在处理期间直接测定湿度和在EO暴露时间直接测定EO浓度的分析仪器(也可见9.5.5和D9.5.5)

— a system controlling the admission of gaseous EO to the chamber;

控制EO气体导入柜室的系统；

— means to demonstrate that gaseous EO is injected into the chamber. This can be done by measuring the temperature of the EO gas flowing from the vaporizer to the sterilizer chamber. This system can control EO concentration during EO exposure time.

证明EO气体已进入柜室的手段。可采用测量从汽化器流入灭菌柜室的EO气体温度的手段。这一系统可控制EO曝露期间的EO浓度。

— means to detect and alert deviations to cycle parameters so that remedial action can be taken in a timely fashion.

测量和警报周期参数偏差的手段，以及时采取补救措施。

c) Aeration area characterization.通风区特征

An aeration area (chamber, cell or room) can be used to remove EO residuals from product/packaging. Temperature uniformity, fresh air make-up and air re-circulation throughout the area are important to ensure consistent and reproducible results. The aeration area should have the following performance and monitoring capabilities:

通风区用于去除产品/包装中的EO残留。整个区域的温度均匀性、新鲜空气补充和空气再循环对确保一致的和可再现的结果是非常重要的。通风区应具备下列性能和监视能力：

— airflow detection equipment, alarm systems or indicators monitoring the air handling system to ensure that it operates within predetermined tolerances and maintains adequate airflow in a loaded room or chamber;

具备空气流量检测设备、报警系统或空气处理系统监测显示器，以保证空气处理系统在满载的房间或柜室内在规定的参数范围内运行，并保持充裕的空气流量；

— equipment to re-circulate air;空气再循环设备；

— means of monitoring room temperature;监测室温的手段

— means of controlling room temperature.控制室温的手段

6.3.2 At a minimum, the specification shall include:

规范至少应包含:

a) description of the equipment, together with any necessary ancillary items, including materials of construction;

设备及其附件，包括组成材料的描述;

b) description of the means by which the sterilizing agent is delivered to the chamber;

灭菌剂进入柜室的方式的描述;

c) description of the means by which any other gas(es), including steam, are delivered to the chamber;

其他气体，包括蒸汽，进入柜室的方式的描述;

d) description of instrumentation for monitoring, controlling and recording the sterilization process, including sensor characteristics and their locations;

用于监视、控制和记录灭菌过程的仪表的描述，包括传感器的特性及其位置

e) fault(s) recognized by the sterilizing equipment;

灭菌设备认可的故障;

f) safety features, including those for personnel and environmental protection;

安全特性，包括人员安全和环境防护;

g) installation requirements, including specifications for required services and requirements for the control of emissions.

安装要求，包括必需的服务和排放控制要求的规范;

D.6.3.2 The equipment specification should be reviewed to ensure that

regulatory and safety requirements are met, technical specifications are appropriate, and services and infrastructure necessary to operate the equipment are available.

设备规范应经审核，以确保规范已满足法规和安全的要求，技术规范是适当的，服务和设备操作所必要的基础设施是适宜的。

The following items should be considered when preparing the equipment specification:

编制设备规范时，应考虑下列内容：

a) If the EO supply to the sterilizer is from a bulk storage tank that is periodically replenished, then the tank should be equipped with a means of removing samples for analysis, a means of emptying the tank of EO and a provision for cleaning in the event of contamination or excessive accumulation of polymers.

如果EO是从定期补充的大体积储存罐内导入灭菌柜的，那么，储存罐就有一个能提取用于分析样品的装置，清空罐内EO的手段，以及在污染或聚合物过度积聚情况下的清洗规范。

b) The system for admission of EO to the sterilizer should be equipped with a vaporizer to prevent liquid EO from being admitted to the sterilizer chamber.

EO导入系统应装配一个汽化器，以防止EO以液态状态进入灭菌柜。

c) The temperature of the EO gas flowing from the vaporizer to the sterilizer chamber should be measured to demonstrate that gaseous EO has been produced.

应测量EO气体从汽化器进入灭菌柜时的温度，以证明进入是气体EO。

d) Steam is utilized to humidify the load and is not intended to be a sterilant. The consistency of steam supply can be determined by the periodic analysis of the boiler feed water or condensate.

蒸汽是用于加湿产品[装载]而不是当作灭菌剂。可通过定期对锅炉加水或冷凝水的分析来确定蒸汽供应的一致性。

e) A minimum of two probes to measure chamber temperature should be used. Large volume chambers can be fitted with more than two probes so as to ensure that the monitoring/control system captures data that reflects the temperature throughout the chamber during use.

至少有二个可以测定柜室温度的探头。大容积的柜室可以安装多于二个探头，以确保监视/控制系统可获得反映柜室工作温度的数据。

NOTE The purpose of two separate probes is to prevent the failure of one sensor from causing an out-of specification process from being erroneously accepted. Comparing two separate temperature sensors will detect that one of the sensors has failed. A dual element temperature probe can be used to meet this need.

注，二个独立的探头是为了防止探头故障而不符合规范的过程被错误地接受。比较二个独立的温度传感器将可以检测其中一个传感器已故障。二个探头可以满足这个需要。

f) It is important to maintain uniform conditions within the sterilizer chamber during processing. This can be achieved by forced gas circulation. If used, a gas circulation system should be equipped with a monitoring device to indicate when circulation is ineffective as devices that solely monitor “power on” to the fan or pump are not sufficient.

在灭菌期间灭菌柜内保持均衡的条件是十分重要的。这可以通过迫使气体循环来达到。如果使用，安装一个带监视装置的气体循环系统，当循环无效或泵力的不足时，监视装置显示器闪动‘power on’。

g) Areas used for storage of cylinders, tanks or cartridges of EO or EO gas mixtures should be secured and ventilated.

用于EO或EO混合气体钢瓶、罐或盒储存的区域应独立和通风。

h) Where ambient conditions are subject to temperature variation greater than the range recommended by the supplier, storage areas for the containers of EO should include provision for temperature control.

如果环境条件可能导致大于供应商推荐的温度变化范围，那么，EO容器的贮存区域应包含一个控制温度的防护措施。

It might not be possible to calibrate controlling and monitoring instruments under actual processing conditions, e.g. humidity sensors. Calibration results for these instruments should be correlated against qualification studies. Processing conditions can have a detrimental effect on some types of sensors, e.g. humidity sensors. Sensors might require replacement after repeated exposure to processing conditions due to irreversible deterioration of materials currently used as sensing elements. It might be necessary to implement a program of more frequent maintenance for these sensors than that recommended by the sensor manufacturer/supplier.

在实际工作条件下，去校验控制和监视仪器也许是不可能的，如湿度传感器。这些仪器的校验结果对验证研究有关联。加工条件可能对一些传感器有不利的影响，如，湿度传感器。反复暴露于加工条件后导致传感元素的材料不可逆的老化后，可以更换传感器。以高于制造商或供应商推荐的保养频率去保养这些传感是必要的。

6.3.3 Software used to control and/or monitor the process shall be prepared and validated in accordance with the elements of a quality system that provides documented evidence that the software meets its design specification.

按质量体系元素的要求，用于过程控制和/或监视的软件应经准备和确认，以提供书面证据证明软件符合其设计规范。

NOTE For further information, attention is drawn to ISO/IEC 90003.

注：进一步信息见ISO/IEC90003。

6.3.4 The means of monitoring and controlling the process variables shall be determined and specified.

应确定和规定监视和控制过程变量的手段

6.3.5 Means shall be provided to ensure that failure in a control function does not lead to failure in recording of process variables such that an

ineffective process appears effective.

应提供适当的手段，以防止某控制功能失效而导致过程参数记录失效，从而致使无效的过程显得有效的。

NOTE This may be achieved either by the use of independent systems for control and monitoring or by a cross-check between control and monitoring which identifies any discrepancies or indicates a fault.

注：可通过使用独立的控制和监视系统或控制和监视之间的相互校验实现该目的，发现矛盾并指出故障。

D.6.3.5 If there is an undetected failure of a control or monitoring function, a sterilization load could be released without having met its required processing parameters. To prevent this from happening, it is general practice to have redundant sensors for many critical process parameters. The common options for utilizing these redundant sensors include:

如果有一个未被发现的控制或监视功能的故障，灭菌产品可能在未满足规定的加工参数的情况下被放行。为了防止此类事件的发生，通常是备用一个那些重要参数的传感器。利用这些备用的传感器的选项包括：

a) use one sensor for control, and another sensor for monitoring and reporting;

用一个传感器用于控制，另一个传感器用于监视和报告。

b) use two sensors, or their average value, for both monitoring and control; this system needs to generate an automatic fault condition if the difference between the two sensors exceeds a defined value;

用二个传感器，或他们的平均值，都用于监视和控制。如果二个传感器的差异超过了规定的限值，系统需产生一个自动的故障条件。

c) use dual element sensors for both monitoring and control; this system needs to generate an automatic fault condition if the difference between the two elements exceeds a defined value.

使用双重的监视和控制传感器。如果二个传感器的差异超过了规定的限值，系统需产

生一个自动的故障条件。

7 Product definition产品定义

7.1 General通则

7.1.1 The purpose of this activity is to define the product to be sterilized, including the microbiological quality of the product prior to sterilization and the manner in which product is packaged and presented for sterilization.

对需灭菌的产品进行定义，包括灭菌前产品微生物质量，及产品包装和提供灭菌的方式。

D.7.1.1 Product definition involves documentation of essential information about the medical device to be sterilized (i.e. the new or modified product).

产品定义涉及到被灭菌医疗器械的必要的信息文件[如是新产品还是改造过产品]

Product definition for a medical device includes the medical device itself, the sterile barrier system containing the device, and any accessories, instructions, or other items included in the packaging system. It also includes a description of the intended functionality of the medical device, and the available manufacturing and sterilization processes. The product definition process should also consider whether this is a new design, or whether it is part of an existing product family.

作为医疗器械的产品定义包括医疗器械本身，装有产品的无菌屏障系统，以及包装系统内的任何附件、说明书或其他部件。也包含医疗器械预期功能和适当的制造和灭菌过程的描述。产品定义过程也应考虑产品是否是新设计的，或者是否是目前产品族的一部分。

The following should be considered as part of product definition:

下列应考虑为产品定义的部分:

a) physical attributes of the medical device (composition and configuration);
医疗器械的物理属性[组成和结构]

b) intended use of the medical device;医疗器械的预期用途

c) whether the medical device is intended for single use or for multiple use;医疗器械预期是一次性使用还是多次使用。

d) design characteristics that would affect the choice of sterilization process (e.g. batteries, fibreoptics, computer chips);可能影响灭菌过程选择的设计特征[如，电池、光纤、计算机芯片]

e) raw materials/manufacturing conditions that could affect microbiological quality (e.g. materials of natural origin);

可能影响微生物质量的原材料/制造条件[如天然材料]

f) required sterility assurance level (SAL);规定的无菌保证水平

g) packaging;包装

h) loading configuration; requirements for a specific load or mixed loading configurations, or range of acceptable loading configurations;

装载方式，规定的装载或混装方式，或可接受的装载方式的范围

i) compatibility with EO or gas mixture and processing conditions (preconditioning, sterilization and aeration processes).

与EO或混合气体和加工条件[预处理、灭菌和通风过程]的兼容性

7.1.2 Product definition shall be performed prior to the introduction of a new or modified product, package or loading configuration. A demonstration of equivalence (with reference to the challenge to the sterilization process) to a previously validated product, package or loading configuration shall be considered to meet the requirement to perform product definition. Any demonstration of equivalence shall be documented.

在引入新的或改造过的产品、包装或装载方式之前，应进行产品定义。应考虑与之前已验证的产品、包装或装载方式的等效性（灭菌过程挑战性）证明，以满足产品定义的要求。任何等效评价应记录。

D.7.1.2 A technical review should be performed to compare the new or modified product to the validated product and/or PCD that was used to validate the existing EO process. The construction and configuration of the new or modified product should be carefully examined for any features that could present obstacles to the penetration of EO, heat or humidity. For medical device manufacturers, this comparison should also involve an examination of factors that could affect the initial bioburden on the product, including the location of the manufacturing facilities, the types of raw material used, the sources of these materials and production methods. For modified reusable products, this comparison should include the evaluation of the cleaning efficacy for the product.

应进行技术评审，以比较新的或改造过的产品与已验证的产品和/或用于验证目前EO过程的PCD，应十分仔细地检查新产品或经改造的产品的结构和构造，以发现任何阻碍EO、热或湿穿透的结构特点。对医疗器械制造商来说，这种比较涉及到能影响产品初始污染菌的各种因素的检查，包括制造机构的地点、使用的各种原材料，材料的来源和生产工艺。对于经改造的可重复使用的产品，比较应包括产品清洗效果的验证。

If a new or modified product is demonstrated to be equivalent to an existing medical device or PCD for which sterilization characteristics are already known, the new or modified product might be considered

to be part of a product family or a processing category.

如果新的或经改造的产品被证明与目前已知灭菌特征的医疗器械或PCD等效，那么，新的或经改造的产品可以考虑为产品族或加工组的组成部分。

NOTE AAMI TIR 28[26] is a useful guide for minimizing the risk of introducing a new or modified product that presents a greater challenge to the sterilization cycle than the product/PCD previously validated.

注，降低介绍与已验证的产品/PCD相比在灭菌周期方面有更大挑战的新的或经改造的产品的风险，AAMI TIR 28[26]是有用的指南。

If the product configuration, density or load configuration of the candidate

product and its packaging could present a greater challenge to the sterilization process than the previously validated product,

then EO, heat and humidity penetration studies and/or cycle lethality studies should be conducted.

如果候选产品的结构、密度或装载方式及其包装与已验证产品相比在灭菌过程方面具有更大的挑战性，那么，应进行EO、热、湿的渗透性研究和/或灭菌周期杀灭能力的研究。

As part of the technical review the following questions should be considered. If the answer to any of the following questions is “yes”, then further evaluation of the new or modified product might be necessary to determine if it is more difficult to sterilize than the previously validated product:

作为技术评审的一部分，应考虑下列问题。如果针对下列问题的回答是‘yes’，那么，可能需要进一步评估新产品或经改造的产品，以证明比已验证的产品是否更难灭菌。

a) with respect to the previously validated product, does the new or modified product:

相对于原来已经验证的产品，新产品或经改造的产品是否:

1) have more restricted passageways or inner chambers;

有更受限制的通道或内部腔间;

2) have fewer openings;更少的开口;

3) have more internal surfaces;有更多的内表面积;

4) have more mated surface areas and/or occluded spaces;有更多的配合面和/或闭塞空间;

5) have more closures;有更多的封闭;

6) have longer or narrower lumens;有更长或更窄的腔道;

7) include changes or differences that could reduce the transfer of heat,

humidity or EO;包括能够减少热、湿或EO转移的变化和不同;

8) have a bioburden or bioburden resistance significantly higher than that of the reference product (due to manufacturing conditions, handling, cleaning process or materials used); or

生物负载数量或生物负载的抗力明显高于基准产品(由于制造条件、处理、清洁过程或材料的使用); 或

9) contain materials or structures that could be adversely affected by the proposed processing or sterilization method;

设定的过程或灭菌方法对含有的材料或结构能产生不利的影响;

b) with respect to the previously validated product, does the packaging of the new or modified product:

相对于已验证的产品, 新的或经改造的产品的包装是否:

1) have any changes in packaging elements, including instructions or protective barriers;

任何包装元素的变化, 包括说明或保护屏障;

2) have any additional impermeable protective barriers (e.g. container, case, template, that would restrict or interfere with EO or humidity penetration or removal);

有任何增加的不透水的保护屏障[如, 容器, 盒子, 基盘, 那些可能限制或干扰EO或湿的渗透或去除]

3) have a change in the porosity of the packaging material, (e.g. basis weight, treatment - adhesive or coating);

包装材料的多孔性的变化, [如, 基本重量, 粘合或涂层处理]

4) have a decrease in the surface area of the venting material or underlying opening (e.g. application of tape or secondary label, change in size of label);

表面通风材料的区域或基层开口的减少

5) increase the bioburden level of the product; or

产品的生物负载水平增加，或

6) change the number of barrier layers?

改变了屏障的层数?

c) with respect to the previously validated product, does the load configuration of the new or modified product:

相对于已验证的产品，新产品或经改造产品的装载方式是否:

1) differ significantly from the validated load configuration of the reference load;

与已验证的基准装载的装载方式明显不同;

2) differ significantly in the amount of absorptive materials;

吸附材料的用量明显不同

3) differ significantly in density from that of the reference load; or

与基准装载的密度有明显不同

4) differ significantly in total load volume.

总的装载体积明显不同

7.1.3 Product shall be designed to allow removal of air, if applicable, and penetration of heat, humidity and EO during the sterilization process, and removal of EO at the end of the process.

产品应设计成允许空气去除，如适用，应考虑灭菌过程中热量、湿和EO的穿透，以及在过程结束阶段的EO去除。

D.7.1.3 The presence of either occluded spaces or mated surfaces should be evaluated in consideration to the designation of an internal PCD that would be used for subsequent lethality qualification studies.

应评估配合面积和闭塞面积二者的存在，评估应考虑到用于随后的杀死力研究的内部PCD的设计；

7.1.4 Packaging shall be designed to allow removal of air and penetration of heat, humidity and EO during the sterilization process, and removal of EO at the end of the process.

产品包装应设计成允许空气去除，以及考虑灭菌过程中热、湿和EO的穿透，以及过程结束时的EO去除。

D.7.1.4 The major function of a sterile barrier system for a sterilized medical device is to ensure that the product remains sterile until used. During sterilization, the sterile barrier system needs to be able to

withstand the process conditions and to remain intact to ensure product quality.

无菌医疗器械的无菌屏障系统的主要功能是确保产品到使用时保持无菌。在灭菌期间，无菌屏障系统应能经受过程条件，并保持完整以确保产品质量。

When selecting a packaging system for a product that is to be sterilized, certain major design and manufacturing factors are considered with respect to the particular sterilization process. To ensure EO penetration, the permeability of the packaging to the particular sterilizing environment is of utmost importance. As air removal is part of the EO sterilization process the packaging system should also allow gases to vent into, and out of, the package during pressure changes during gas injections and evacuations without damage to, or rupture of, the seal integrity.

选择计划灭菌产品的包装系统时，相对于特定的灭菌过程，要考虑某些主要设计和制造因素。为确保EO的穿透，针对特定的灭菌环境的包装的穿透性尤为重要。当空气去除是EO灭菌过程的部分时，包装系统应允许气体进出，气体进出引起压力变化时，包装应不会受损伤、破裂，封口完整。

The ability of the sterile barrier system (SBS) to protect product during customary handling and distribution should be demonstrated. Evidence should

also be generated to show that the SBS can withstand the sterilization process without losing its ability to protect the product. Validation of the SBS should consider the potential stresses that the SBS can be exposed to during an EO sterilization process. Considerations would include vacuum/pressure levels, rate of pressure change, temperature, etc. It is common practice to demonstrate suitability of the SBS by exposure of the SBS to multiple sterilization processes (see D.7.2.1 and D.7.2.2).

应评估常规操作和货物转移时无菌屏障系统防护产品的能力。应有证据证明无菌屏障系统能经受灭菌过程而未失去保护产品的能力。无菌屏障系统[SBS]的确认应考虑潜在的SBS暴露于EO灭菌过程时的应激状态。考虑可能包括真空/压力水平、压力变化的速率、温度等。通常的做法是通过将SBS多次暴露在灭菌过程以证明SBS的适应性(见D.7.2.1和D.7.2.2)

Packaging considerations are addressed in more detail in the ISO 11607-1 and ISO 11607-2.

包装的考虑因素在ISO11607-1和ISO11607-2中有详细的描述。

7.1.5 The load configuration shall be designed to allow removal of air and penetration of heat, humidity and EO during the sterilization process, and removal of EO at the end of the process.

产品装载方式应被设计成允许空气去除，和灭菌过程中热、湿和EO的穿透，以及过程结束时的EO去除。

D.7.1.5 The load configuration in the chamber can influence product heat, humidity, EO gas penetration and EO gas removal. The load configuration is to be defined during the validation to ensure adequate product temperature, humidity and EO penetration and EO removal during processing.

柜室内的装载方式能影响产品的热、湿、EO的穿透和EO的去除。确认时应定义装载方式，以确保在过程期间产品温度、湿度和EO渗透和EO去除是充分的。

7.1.6 It shall be demonstrated that the specified sterilization process is effective in sterilizing the most difficult-to-sterilize location within the

product. This can be achieved by performing process definition and validation of a new product; or through the demonstration of equivalence to a previously validated product, or internal process challenge device (internal PCD) used to qualify the product SAL when exposed to the specified sterilization process (See 8.6 and D.8.6).

应证明规定的灭菌过程对产品最难灭菌部位的灭菌是有效的，这可以通过进行过程定义和新产品确认来获得；或者通过与已确认产品的等效性证明，或者用内部PCD通过规定的灭菌过程来证明能满足产品SAL的要求(见8.6和D8.6)；

D.7.1.6 A PCD is a device into which a microbiological challenge is located. Examples of ways to develop PCDs for use in the demonstration of equivalence include, but are not limited to

PCD是一种放入微生物挑战的器具。用于等效性证明的PCD制作的方法示例，但不仅限于：

a) placement of a microbiological challenge between rings, lands, grommets or ribs of a syringe stopper,

将微生物挑战放在注射器内，

b) placement of a microbiological challenge in the middle of the lumen of a tube that is then reconnected using a solvent bond agent or a connector to restore product integrity,

将微生物挑战放在窄的管腔中间，然后把管用溶剂粘合剂或连接器再连接起来，恢复产品的完整性，

c) placement of a microbiological challenge in an interface,

将微生物挑战放在一个接口中

d) placement of a microbiological challenge in a series of envelopes or packages.

将微生物挑战放在各种信封或袋子中

Several PCD designs have been recommended for use in health care facilities.

已有几种PCD推荐给医疗保健机构使用。

NOTE For further information see ANSI/AAMI ST41. See also D.8.6 for further information about internal and external PCDs.

注，进一步的信息见ANSI/AAMI ST41。有关内部和外部PCD的进一步信息见D.8.6。

To prepare the internal PCD, the microbiological challenge can be inoculated on the product either directly or indirectly. Direct inoculation is accomplished by applying a liquid suspension of the spores on the product. Indirect inoculation is accomplished by placing an inoculated carrier either within the package or in/on the product.

将微生物挑战直接或间接接种在产品上，来制作内部PCD。直接接种可在产品上涂抹孢子悬浮液。间接接种可将染菌载体放在包装内，或产品内/上。

Listed below are various ways to prepare a PCD.

下列给出的是各种制作PCD的方法。

a) *Inoculated product:* the product to be sterilized is used to prepare the PCD and is inoculated directly or indirectly.

染菌产品：采用需灭菌的产品制作 PCD，直接或间接的接种到产品上。

b) *Inoculated simulated product:* a simulated product is used to prepare the PCD and is inoculated directly or indirectly. The simulated product consists of portions of a medical device or a combination of components that are known to represent the greatest challenge to the process while still adequately representing all products within a product family.

染菌模拟产品：采用一模拟产品制作 PCD，直接或间接的接种到模拟产品上。模拟产品可以由某一医疗器械的几部分组成，或是一些部件的组合， 这些部件对灭菌工艺的监测性要求最高，同时可充分代表 EO 产品族中的所有产品。

c) *Inoculated object:* such as a package, piece or tubing, that is used to

prepare the PCD and is directly or indirectly inoculated.

染菌载体：用诸如纸条、圆盘或其它基质作载体制作PCD，可直接接种到载体上。

NOTE Direct inoculation with a spore suspension can result in variable resistance of the inoculated product because of surface phenomena, other environmental factors and the occlusion of the spores on or in the product. Therefore, it is important to provide scientific rationale or validation for this practice to ensure that the resistance of the inoculated product is reasonably correlated to the routine product. The inoculum recovery should also be validated if resistance is measured by plate count techniques. See Gillis and Schmidt,[30] West[40] and ISO 11737-1 for additional information.

由于表面现象，及其它环境因素和孢子在产品上或产品内的吸留，会导致被移植产品的移植孢子悬浮液的抗力变化。 所以，重要的是要为本实践提供科学根据或进行确认，以确保被接种模拟产品的抗力与原产品具有合理相关性。若采用平皿计数技术测量抗力，则必须确认接种物回收率。详见 Gillis 和 Schmidt[14]、West[22]、和 ISO 11737-1。

A means of demonstrating equivalence to a previously qualified product or internal PCD is the comparison of the relative rates of inactivation of BIs placed in a challenge location within the new or modified product and previously qualified product/master product(see D.8.6 and D.12.5.2) when both are exposed to a fractional cycle. Equivalence studies should compare the new or modified product to the internal PCD used to validate the process. If a PCD is used for this comparison, this resistance of the PCD should be assessed as part of the annual review.

证明与先前合格产品或内部PCD等效的手段是通过，同时暴露于短周期的、分别放于新产品或经改造产品与已合格产品或主产品中挑战位置的BI的相对失活率的比较。等效研究应比较新产品或经改造产品与用于验证过程的内部PCD。如果PCD用于比较，在年度审核时应对PCD的抗力进行评估。

7.2 Product safety, quality and performance 产品安全、质量和性能

7.2.1 It shall be confirmed that the product and its packaging meet specified requirements for safety, quality and performance following the application of the defined sterilization process using the process parameter tolerances that have been determined to have the greatest impact on the product/package.

应确认在对产品/包装具有最大挑战性的过程参数下，在经过规定的灭菌过程后，产品及其包装的安全、质量和性能符合规定的要求。应考虑过程参数公差的影响。

NOTE Design control is one aspect addressed in ISO 14971.

ISO14971中的设计控制为一个方面

D.7.2.1 It is important to select materials that tolerate the chemical and physical changes caused by EO and/or any diluents over the anticipated range of sterilization conditions. Properties of materials required to satisfy requirements for product performance, such as physical strength, permeability, physical dimensions and resilience, are evaluated after sterilization to ensure that the materials are still acceptable for use. Degradation effects due to exposure to the sterilization process, such as crazing and embrittlement may need to be considered. Where applicable, the effects of exposure to multiple sterilization processes may also need to be evaluated.

选择的材料应能耐受，在预期的灭菌条件范围条件下，由EO和/或任何稀释剂引起的化学和物理变化。满足产品性能要求的材料性能，如物理强度、渗透性、物理尺寸和弹性，灭菌后应验证，以确认选择的材料用于使用仍是可接受的。需要考虑灭菌过程后的降解效果，如裂纹和脆化。应验证多次灭菌对材料的影响。

Demonstration that the specified sterilization process does not affect the correct functioning of the product can be accomplished by performing functionality tests, or other appropriate tests, on the medical device and its packaging system. These tests can be performed after exposure in the sterilizer or other environmental chambers that simulate the specified process and can range from a simple visual inspection to a battery of specialized tests.

通过产品操作的试验，或其他适当的试验，可以证明特定的灭菌过程未影响医疗器械

及其包装系统的正常功能。在灭菌柜或与特定灭菌条件相似的柜室灭菌后进行产品试验，可能是对样品的一组特定的外观检查。

Elements that could affect safety, quality or performance include:

可能影响安全、质量或性能的因素包含:

a) cycle pressure changes that could affect the sterile barrier system seal integrity;

灭菌周期的压力变化可影响无菌屏障系统的封口完整性;

b) effects of EO exposure time, temperature, humidity and, if applicable, any diluent gases present in the intended sterilization mixture;

EO暴露时间、温度、湿度，以及用于混合气体的稀释剂。

c) inclusion of new materials known to retain higher EO residuals;

已知的具高EO残留的新材料的包容性?;

d) packaging characteristics;包装特性

e) the presence of lubricants, especially within mated surface areas;

润滑油的存在，特别是在结合面部位;

f) whether the medical device requires disassembly or cleaning;

医疗器械是否要求拆卸或清洗;

g) safety hazards (e.g. leachable materials, or batteries or sealed liquids that could leak or explode);

安全危害[如，浸出物质，或电池或密封液体的泄漏或爆炸]

h) number of sterilization cycles.

灭菌周期的次数;

Medical devices containing a potential source of ignition (e.g. a battery) should be sterilized using a process that does not contain an explosive mixture

of EO in any part of the cycle.

含有潜在点火源(如电池)的医疗器械在任何灭菌过程中应使用不含可爆炸的EO混合物进行灭菌。

7.2.2 If multiple sterilization cycles are permitted, the effects of such processing on the product and its packaging shall be evaluated.

如允许使用多次灭菌周期，则应评价此类处理对产品和其包装的影响。

D.7.2.2 The evaluation of multiple sterilization cycles can be performed utilizing the routine sterilization process for the product/package. The effect of repeated sterilization and any necessary pre-treatment on the materials, functionality and safety of the product should be evaluated.

应用常规灭菌过程来进行多次灭菌周期的产品/包装评介。应评价重复灭菌和任何必需的前处理对产品的材料、功能和安全的影响

For reusable medical devices, the manufacturer's reprocessing instructions should be available and followed. The instructions should include the recommended sterilization parameters for the process and the limits to the number of sterilization cycles to which the reusable medical device can be exposed. If applicable, testing and inspection should be performed to assess functionality of the reusable medical device following sterilization. The medical device manufacturer's claims for the number of allowable cycles should be considered to be the maximum. A system should be in place which will provide notification if the maximum number of cycles is reached.

对可重复使用的医疗器械，应有制造商的再处理说明，并应遵照说明书。说明书应包括推荐的灭菌参数和极限灭菌周期次数。如适用，灭菌后应对再使用的医疗器械进行测试和检验，评估其功能性。医疗器械制造商所主张的允许周期次数应视为最高次数。必须配有能在达到最高周期次数时给出通知的系统。

NOTE See ISO 17664 for more information.

7.2.3 The biological safety of product following exposure to the sterilization

process shall be established in accordance with the applicable parts of the ISO 10993 series.

应按照适用的ISO10993系列标准对暴露于灭菌过程后产品的生物学安全评价

7.2.4 Means shall be established to reduce EO residual levels such that the processed products comply with the requirements of ISO 10993-7.

应建立减少EO残留量的手段，使经灭菌的产品满足ISO10993-7的要求；

D.7.2.4 Proper aeration is essential to control EO residues in medical devices after EO processing. Consideration should be given to the placement of the residual product test samples within the load, taking into account the most challenging positions for EO removal.

用适当的通风来控制EO加工后医疗器械的EO残留是必要的。需要考虑的是，用于EO残留量试验的产品在装载中的位置，这个位置应是EO去除最具挑战性。

Local environment, health and safety regulations can require extra worker exposure precautions when handling EO sterilized products even when product residuals are in compliance with ISO 10993-7 requirements.

当处理灭菌产品，甚至在处理EO残留已符合ISO10993-7要求的产品时，当地的环境、健康和安全法规可能要求额外的工人防护措施。

For health care facilities: If information regarding aeration for a medical device is not available from the manufacturer, the health care facility should establish the aeration process for that device using either data or knowledge of the product and its material and design. The aeration process should be established based upon the most difficult-to-aerate product or product family.

对医疗保健机构：如果由制造商来提供医疗器械关于通风的信息是不适当的，医疗保健机构应利用产品的数据、知识、材料和设计为该器械确定通风过程。按最难通风的产品或医疗器械来确定通风过程。

7.3 Microbiological quality 微生物质量

7.3.1 A system shall be specified and maintained to ensure that the

microbiological quality and cleanliness of the product presented for sterilization is controlled and does not compromise the effectiveness of the sterilization process.

应规定和保持一个体系，以确保灭菌产品的微生物质量和清洁是受控制的，而且不会影响灭菌过程的效果；

NOTE Bacterial endotoxins are not destroyed by the ETO process. Guidance on testing for bacterial endotoxins is provided in ANSI / AAMI /ST72 and the applicable pharmacopeia.

注，EtO过程不能消除细菌内毒素， ANSI / AAMI /ST72和适用的药典对内毒素试验提供了指南。

D.7.3.1 Guidance on testing for bacterial endotoxins is provided in ANSI/AAMI/ST72 and the applicable pharmacopeia.

ANSI/AAMI/ST72和相关的药典中提供了细菌内毒素试验的指南。

7.3.2 For single use medical devices, an estimation of bioburden at a defined interval shall be performed in accordance with ISO 11737-1. For reusable medical devices, an assessment of the effectiveness of the specified cleaning process and, if applicable, disinfecting process, shall be performed.

按ISO11737-1的要求，应定期对一次性使用医疗的生物负载进行评估。对重复使用的医疗器械，应对规定的清洗过程和消毒过程(如果适用)的有效性进行评价；

NOTE Requirements for information to be provided for the reprocessing of resterilizable devices are given in ISO 17664. Information for the assessment of the effectiveness of cleaning and disinfection processes is given in the applicable parts of ISO 15883 series.

注：ISO 17664给出了可重复灭菌器械的再处理所需提供信息方面的要求。ISO15883系列标准的适当内容描述了清洗和消毒过程有效性评价的信息。

D.7.3.2 In health care facilities, attention to microbiological quality will comprise having strict procedures for collection and handling of used,

reusable medical devices, and for validation and control of the cleaning processes for reusable medical devices in accordance with the medical device manufacturer’s instructions.

在医疗保健机构，微生物质量将包括严格的可重复使用医疗器械的收集和处理的过程，以及可重复使用医疗器械的清洗过程的控制和验证要符合医疗器械制造商的说明。

When using the bioburden approach (see Annex A) bioburden testing should be performed at least quarterly. The period of monitoring can be extended following a documented risk analysis that considers the following: the use of product families, historical data, statistical analysis, manufacturing frequency and product design.

如果采用生物负载方法[见附录A]，至少每季进行一次生物负载试验。监视的周期可以根据文件化风险分析来确定，可考虑下列内容:产品族的使用、历史数据、统计分析、制造频率和产品设计。

7.4 Documentation 记录

The results of product definition shall be documented by the manufacturer of the device.

产品定义的结果由器械制造商记录。

D.7.4 Upon completion of the product definition the following should be documented:在产品定义完成后，下列内容应记录:

a) a description of the product configuration and how it is to be presented to the EO process (packaging and load configuration). The specification should also include or reference the required SAL, as well as evidence for, or assessment of, the compatibility of the product with the process.

产品状态的描述和提供灭菌时状态(包装和装载方式)。规范应包含或参考要求的SAL，及产品对灭菌工艺的适宜性的证据或评估。

b) the result of the comparison between the new or modified product and the

existing validated product(s). This result should clearly demonstrate that product complexity, materials, packaging and load configuration were assessed.

新产品或经改造的产品与目前已验证产品的比较结果。比较结果应清楚地表明评价产品的复杂性、材料、包装和装载方式。

c) evidence or assessment of the bioburden of the product and its resistance relative to the internal PCD.

产品生物负载及其与内部PCD抗力比较的证据和评估。

d) the documented conclusion that the new or modified product is suitable for adoption into the product family/processing category specifically referenced in the current validation study to achieve the specified SAL. This conclusion should include or reference any results from additional tests performed to supplement the existing validation study and any further testing performed for confirmation/qualification for routine release of product from the existing validated cycle (i.e. residual testing, functional testing).

根据当前可达到规定的SAL的确认研究得出的新产品或改造过产品适合归入产品族/加工类型的文件化的结论。 该结论应包括或参照为补充现有确认研究所做的附加试验的结果，为证实和鉴定现有确认的灭菌周期中产品的常规放行所做的进一步的测试的结果 (如残留测试，功能性测试)。

This documentation should be approved, retained and retrievable.

这些文件应批准、保存和可检索的。

8 Process definition过程定义

8.1 The purpose of this activity is to obtain a process specification which can be applied for the sterilization of the defined product (see Clause 7) during the validation studies.

在灭菌确认期间，为已定义产品的灭菌提供一个过程规范。

8.2 The sterilization process applicable for the defined product shall be

established. The defined product includes new or modified product, packaging or loading configurations.

应建立定义产品适当的灭菌过程。定义产品包含新的或改动过的产品、包装或装载方式。

D.8.2 The result of the process definition activities is a detailed specification of a sterilization process. The selection of the sterilization process that is to be used for medical devices should include consideration of all factors that can influence the efficacy of the process. The following should be taken into account:

过程定义活动的结果是详细的灭菌过程规范。用于医疗器械灭菌过程的选择应包含能影响过程效果的所有因素的考虑。文档应有下列内容:

— availability of sterilization equipment;

灭菌设备的适用性;

— range of conditions that can be achieved within the available sterilizing equipment;

适用的灭菌设备内能达到的条件范围;

— sterilization processes already in use for other products;

已用于其他产品的灭菌过程;

— sterilant to be used (i.e. 100 % EO or EO mixed with diluent gas);

使用的灭菌剂[如，100%或混合有稀释剂的EO]

— product limitations (i.e. temperature, humidity, pressure sensitivity);

产品局限[如，温度、湿度、压力敏感性]

— requirements for levels of residual EO and/or its reaction products;

EO和/或反应产物的残留水平的要求

— results of process development experiments.

过程开发试验的结果

During process definition, a manufacturer will use microbiological testing and other analytical tools to help establish an appropriate sterilization process for a medical device.

在产品定义期间，制造商将使用微生物试验和其他分析工具帮助建立一个合适的医疗器械灭菌过程。

The sterilization process parameters to be established include:

灭菌过程参数应包括：

a) temperature range within the preconditioning room (if used);

预处理室内[若使用]的温度的范围

b) relative humidity range within the preconditioning room (if used);

预处理室内[若使用]的相对湿度的范围

c) time set point and range within the preconditioning room (if used);

预处理室内[若使用]的时间设定点及其范围

d) vacuum and pressure levels and rates of pressure changes in the sterilization chamber;

灭菌柜内真空和压力水平及其压力变化范围；

e) if used, confirmation that chamber recirculation operational during sterilant dwell;

若采用，灭菌剂住留期间的灭菌柜再循环操作的确认；

f) temperature set point and range within the sterilization chamber;

灭菌柜内的温度设定点及范围

g) humidity control set point (pressure or %RH) and range within the sterilization chamber environment;

灭菌柜环境内的湿度控制设定点[压力或%RH]及范围

h) EO and diluent gas (if used) injection pressure set point and range; this will include EO concentration if EO analysis equipment is installed on the sterilization chamber;

EO及其稀释剂注射压力设定点及范围;如果EO分析设备安装在灭菌柜,还包含EO浓度。

i) EO dwell time; EO住留时间

j) setting for the in-chamber gas flushing prior to the removal of the load from the sterilization chamber (if used);

产品移出灭菌柜前的柜内气体清洗的设定;

k) temperature set point and range within the aeration room (if used);

通风室内温度设定点及范围[若使用]

l) time set point and range within the aeration room (if used);

通风室内时间设定点及范围[若使用]

m) air flow/changes parameters.

空气流动/变化参数

NOTE For reference in the development of sterilization processes, Annexes A and B provide requirements for determination of cycle lethality.

注，灭菌过程开发的参考，附录A和B提供发灭菌周期杀死率测量的要求。

For health care facilities, for reusable medical devices that will be reprocessed in the health care facility, the manufacturer is expected to provide validated reprocessing instructions, which are based in part on the process definition. It is then the health care facility’s responsibility to review this documentation and confirm that it can follow the medical device manufacturer’s instructions using its own equipment and sterilization processes. The health care facility’s purchasing procedures should require that, prior to the purchase of an EO-sterilizable medical device, the

reprocessing instructions be evaluated to confirm that the device is compatible with the equipment and sterilization processes that are in use at the facility. See also ISO 17664.

对于医疗保健机构，在医疗保健机构将再加工的可重复使用的医疗器械，制造商提供验证过的基于过程定义的再加工说明。审核制造商提供的文件和用自己的灭菌柜和灭菌过程来实施制造商的说明的合适性是医疗保健机构的责任。在EO灭菌医疗器械采购前，医疗保健机构的采购程序应要求经评价的再加工说明，采购产品应兼容目前采用的灭菌工艺和灭菌设备。

If the medical device or packaging manufacturer supplies instructions for reprocessing that are not specific enough or not appropriate (e.g. an EO process with 100 % EO, where the health care facility uses a mixture of EO and diluent gas), the facility should either perform a validation or assess the appropriateness of its own reprocessing method, based on materials effect data and reprocessing instructions for other devices. If the health care facility is not able to validate the product or assess the appropriateness of its own reprocessing method, it should not reprocess the medical device.

如果医疗器械或包装制造商提供的再加工的说明书是不充分的或不适用(如用100%的EO过程，但医疗保健机构使用的是EO混合气体),医疗保健机构应进行确认，或评估自己的再加工方法的适合性，基于其他医疗器械再加工说明和材料影响数据。如果医疗保健机构不会确认这个产品或评估用自己再加工方法的合适性，那么，医疗保健机构不得再加工这个医疗器械。

8.3 Process definition activities shall be performed in a sterilization chamber (developmental chamber or production chamber) that has undergone Installation Qualification (IQ) and Operational Qualification (OQ) procedures (see 9.2 and 9.3).

过程定义活动应在经过IQ和OQ过程的灭菌柜(研发柜或生产柜)内进行。

D.8.3 A developmental chamber is usually a smaller vessel than the production chamber and can be used to perform studies to support validation.

研发性灭菌柜通常比生产性灭菌柜小，但能用于进行研究以支持确认。

Using a developmental chamber does not preclude confirmation of PQ in a production chamber

使用研发性灭菌柜不能替代生产性灭菌柜的PQ确认。

8.4 Documentation and records shall support the validity of process parameters and associated process variables as defined in the process characterization (see 6.2)

文件和记录应支持过程特性(见6.2)中规定的过程参数以及相关过程变量的有效性。

D.8.4 When establishing process definition it is important to consider the impact of the selected processing parameters and their tolerances on the safety and functionality of the product and its packaging. As there are a number of parameters within a sterilization process, (temperature, humidity, pressure changes/rates, EO concentration and time), it is impractical to assess the tolerances of all combinations of all variables. A determination should be made as to which variables will have the greatest impact, and those should be assessed.

当规定过程定义时，考虑选择的过程参数和它们的公差对安全和产品及其包装功能的影响是十分重要的。当灭菌过程有许多参数时，[温度、湿度、压力变化/速率、EO浓度和时间]，评价所有变量组合的公差是不彻实际的。应当有一个结论，明确影响最大的变量，且已评估。

Data supporting this activity can be collected from alternative studies, e.g. product and its packaging validations, product and its package stability test studies, accelerated aging studies, etc. Alternatively, data can be generated from a specific challenge cycle(s) in a developmental or production chamber.

可以从替代的研究中选择支撑这个活动的数据，如，产品及其包装确认，产品和包装适应性试验研究，加速老化研究等。另外，数据可以从研发性或生产性柜室的规定的挑战周期中产生。

8.5 The rate of microbiological inactivation provided by the specified sterilization cycle for a specific microbiological challenge shall be determined, using one of the methods described in Annexes A or B or by an alternative method that demonstrates the product has achieved the required sterility assurance level (SAL).

用附录A或B描述的方法之一或用证明产品已经达到了要求的无菌保证水平的替代方法，测定规定的微生物挑战物经定义的灭菌周期灭菌后微生物失活的概率。

8.6 Biological indicators (BIs) used as part of the establishment of the sterilization process shall

用于灭菌过程单元的微生物指示剂，应:

a) comply with ISO 11138-2:2006, Clause 5 and 9.5,

符合ISO11138-2：2006，5和9.5章节的要求

b) be shown to be at least as resistant to EO as is the bioburden of product to be sterilized, and

对环氧乙烷抵抗力至少与被灭菌产品的生物负载相等；和

c) be placed within an appropriate PCD.

放置于一种适当的PCD内

The appropriateness of the PCD used for process definition, validation or routine monitoring and control shall be determined. The PCD shall present a challenge to the sterilization process that is equivalent or greater than the challenge presented by the natural bioburden at the most difficult to sterilize location within the product.

应测定用于过程定义、确认和日常监视和控制的PCD的适用性；PCD对过程的挑战性应大于或等于产品中最难灭菌部位。

NOTE For information on the selection, use and interpretation of biological indicators, see ISO 14161.

注：生物指示物的选择、使用和分析方面的信息见ISO14161。

D.8.6 A number of approaches can be used to show that the BI is appropriate.

可以用许多方法来表明BI是合适的:

Approach 1 途径1

This approach is to use the rationale that most of the microorganisms found on product present a lesser challenge than the reference microorganism. This approach is applicable when

这个途径是用产品上的大部分微生物的挑战性比基准微生物低的原理。这个途径是适用的，当

a) the BI used in the PCD is in accordance with ISO 11138-2:2006, Clause 5 and 9.5, and

用于PCD的BI符合ISO11138-2：2006的5和9.5条款,和

b) the product bioburden is consistent, and is not likely to contain highly resistant microorganisms.

产品的生物负载是一贯的,不太可能包含高抵抗力的微生物.

In this approach, bioburden trending data should be available and should demonstrate the consistency of the bioburden regarding the number and types of microorganisms. Manufacturing processes and product contact materials should also be evaluated to ensure that potential sources of bioburden are identified and controlled.

在这个方法中,生物负载趋势的数据应是可得到的,并应证明生物负载的微生物种类和数量的一贯性.

Approach 2 途径2

This approach is to use a test of sterility of the product and PCD, following a fractional cycle. The results of this study should provide a means of lethality comparison using survival data from the tests of

sterility for the product and PCD.

这个途径是利用，在短周期下,产品和PCD的无菌试验。这个研究的结果应提供一个用产品和PCD无菌检查存活数据进行杀死力比较的方法。

Typically in this approach, product tests of sterility samples and BI/PCD are exposed to fractional cycle(s) with the intent of achieving negative growth for all product tests of sterility and survivors of the test microorganism from the BI/PCD.

通常情况下，将产品无菌检查的样品和BI/PCD暴露于短周期，这个短周期能达到所有的产品无菌试验为阴性而BI/PCD微生物的试验存活的意图。

Approach 3 途径3

This approach can be applied in cases where 这个途径能应用在

a) the product bioburden challenge is equal to or greater than the challenge of the BI within the PCD,

产品的生物负载的挑战等于或高于PCD内BI的挑战。

b) the product bioburden contains highly resistant microorganisms, or

产品的生物负载包含高抵抗力的微生物，或

c) where a BI with a lower population than required by ISO 11138-2:2006, 9.3 is used in the PCD.

PCD使用的是低于ISO11138-2:2006规定的数据的BI

In this third approach, the lethality challenge of the bioburden and the PCD can be based on direct enumeration methods and/or fraction-negative methods. (See ISO 14161).

在这第三种途径中，用直接计算法和/或短周期阴性法检测产品生物负载和PCD杀死力挑战。

If there is an indication that the challenge posed by the product bioburden exceeds that of the PCD (i.e. if the PCD is not appropriate), one of the

following can be used:

如果出现产品生物负载的挑战性超过PCD[如,如果PCD不适当],可以用下列方法之一:

a) select a BI to use within the PCD having a higher population and/or resistance;

选择一种具有高数量和/或抗力的BI用于放入PCD内;

b) the product can be pre-treated before sterilization to reduce the bioburden numbers;

在灭菌前先处理产品以减少生物负载的数量;

c) the product, the process or both can be evaluated to determine how to reduce the bioburden number or resistance (e.g. by changing the raw materials or manufacturing process used, by improving the manufacturing environment, or by modifying the product design)

确定如何减少产品、工艺过程或二者的生物负载的评估[如通过改变原材料或生产工艺，通过生产环境的防护，或通过更改产品设计]

d) develop a new PCD.

开发一个新的PCD.

If any of the above changes are made, it is important to verify the effectiveness of the changes.

如果出现任何上述变化，验证这些变化的有效性是十分重要的。

Product design might not allow a BI to be positioned in the most difficult-to-sterilize location of the product. In this circumstance it might be appropriate to place the BI in a location to which the relationship with the most difficult-to-sterilize location can be established. Additionally, in many medical devices the most difficult-to sterilize location contains a low number of microorganisms, and therefore the challenge population may be more closely linked to the bioburden of the product.

产品设计可能无法将BI放到产品最难灭菌的部位。在这种状况下，将BI放到一个已确定与最难灭菌部位有关联的部位是适当的。另外，在许多医疗器械的最难灭菌部位内往往含有较少的微生物，尽管如此，挑战力与产品生物负载有紧密的关联。

Different types of PCDs are described in D.7.1.6. Methods similar to those used for determining the appropriateness of the BI can be used for determining the appropriateness of the PCD. A PCD located within the confines of the product, in the product shipper or product shipper case is an internal PCD, whereas a PCD located between shipper cases or on the exterior surfaces of the sterilization load is an external PCD. Internal PCDs can be used for routine product release; however, external PCDs are usually used as they are easier to recover after completion of the sterilization process. Studies conducted in a development chamber can be used to demonstrate the comparative lethality challenge of the internal and external PCDs; however, consideration should be given to the effects of load volume and production sterilizer performance when performing these studies. If the development chamber is not capable of duplicating the production process then the comparative lethality challenge studies should be conducted in the production chamber.

在D7.1.6中描述了各种类型的PCD。 与用于确定生物指示物适宜性的类似方法可用来确定PCD的适宜性。 位于在产品内，或发货包装，或销售包装内的PCD常被称为内部PCD；然而，外部PCD通常是灭菌过程中易被发现的。在试验性柜室内所做的研究可以用来证明内部PCD和外部PCD杀死力挑战的比较。 然而，进行这样的研究时，需考虑装载体积和生产性灭菌柜特性的影响。应对需验证的特定的生产用灭菌器和负载摆放的影响进行评估。 如果试验性柜室没有体现生产过程的能力，那么，应在生产性柜室内进行杀死力挑战比较的研究。

The comparative lethality challenge of the internal versus external PCDs can be assessed using concurrent exposure(s) in a fractional cycle(s). The resulting data can be used for:

用同时暴露于短周期的方法来评估内部PCD和外部PCD的杀死力挑战的比较。这结果数据能用于：

a) making decisions about which internal PCD is appropriate to validate the sterilization process;

展开内部PCD用于验证灭菌是适当的讨论；

b) evaluating candidate designs for external PCDs (i.e. for routine monitoring of the process);

评估外部PCD的设计[如，用于日常的过程监视]。

c) assessing the equivalence of new or modified products for adoption into a validated sterilization process; or

评估经确认的灭菌工艺对新产品或改造过产品的等同性

d) deciding if a new or modified product or internal PCD should become the master product for a product family or processing group.

决定新产品、或改造过产品、或监测器材可成为 EO 产品族的主要成员。

There can be instances when it is desirable to compare the lethality challenge of one PCD to another without comparing both to the challenge of the product. This is often used when an internal PCD has been proven to be appropriate and an external PCD is being introduced for monitoring routine production cycles for conventional release or when it is desirable to change to another external PCD. In this case, a method of evaluating the appropriateness of the PCD is to demonstrate that the external PCD presents an equal or greater lethality challenge when compared to the internal PCD. Typically this is done by performing a single fractional cycle that compares the fraction-negative results of the internal and external PCDs. If the lethality challenge of the external PCD is less than the lethality challenge of the internal PCD (not more than 20 %, United States Pharmocopeia Biological indicators for Ethylene Oxide Sterilization), the PCDs may be considered equivalent since this is the confidence level of the biological indicator used within the PCD.

可能会有这种情况， 不与产品的抗力进行比较，但需要比较两个PCD的抗力。特别是

当一个内部PCD已被证明是适当的，又打算引入一个新的外部PCD时。在这种情况下，证明PCD适宜性的方法其实就是和内部PCD比较，证明外部PCD的抗力等于或高于内部PCD。如果外部PCD的相对抗力小于内部监测器材相对抗力（不多于 20％），两个装置可视为是等同的。

NOTE It is not uncommon to find an external PCD in a less difficult-to-sterilize configuration presenting a greater lethality challenge than an internal PCD in a more difficult-to-sterilize configuration. It is theorized that this occurs because the EO is removed more rapidly from the external PCD than the internal PCD, resulting in less gas exposure time to the microbiological challenge.

注：出现在灭菌困难程度较低的结构中的外部PCD的抗力高于在灭菌困难程度较高的结构中的内部监测器材的情况也并非是不寻常的。 从理论上讲，这是因为EO 从外部PCD中排出要比从内部PCD中排出快得多，造成外部PCD中微生物在气体中曝露的时间要短一些。

8.7 Commercially supplied biological indicators used in the definition of the sterilization process shall comply with the requirements in 8.6 and all applicable clauses of ISO 11138-1.

用于灭菌过程定义的市售的生物指示物应符合8.6条款和ISO11138-1适用条款的要求。

8.8 If chemical indicators are used as part of the definition of the sterilization process, these shall comply with ISO 11140-1.

如果灭菌过程定义使用化学指示物，则应符合ISO11140-1的要求。

Chemical indicators shall not be used as the sole means of establishing the sterilization process and shall not be used as an indicator that the required SAL has been achieved.

化学指示剂不可作为建立灭菌过程的唯一方式，也不应被用作规定的SAL已达到的指示剂。

8.9 If tests of sterility are performed during the definition of the sterilization process, they shall comply with ISO 11737-2.

如果灭菌过程定义期间需进行无菌检查，则应符合ISO11737-2的要求。

9 Validation 确认

9.1 General 通则

9.1.1 The purpose of validation is to demonstrate that the sterilization process established in the process definition (see Clause 8) can be delivered effectively and reproducibly to the product within the sterilization load. Validation consists of a number of identified stages: installation qualification (IQ), operational qualification (OQ) and performance qualification (PQ). Testing shall not commence until the procedures and/or protocols have been approved.

确认的目的在于证明建立于过程定义之上的灭菌过程可以有效地和持续地对灭菌装载内的产品提供灭菌过程。确认由多个定义的阶段组成:安装验证，操作验证和性能验证。在试验开始前，确认流程或方案应经批准。

D.9.1.1 The object of validation is to document the evidence required to provide a high degree of assurance that a specific process will consistently produce product meeting the required sterility assurance level (SAL). Product sterilized in the validated process should be shown to meet predetermined specifications and quality characteristics related to product functionality and safety (i.e. through product compatibility studies).

确认的目的就是证明一个特定的过程能始终如一地生产出符合要求无菌保证水平要求的产品的证据。经过业已确认的灭菌工艺灭菌和产品应能满足与产品功能性和安全性相关的预定的规范和质量特征 (如，通过产品的适用性研究)。

Validation of the sterilization process should be performed according to an approved written document (e.g. protocol) that defines the testing procedures and the acceptance criteria, prior to initiation of testing. This document should be reviewed by a sterilization specialist(s).

灭菌过程的确认应按照在试验开始前经批准的已规定试验程序和接受准则的书面文件（如，方案)进行。该文件应由一名或多名灭菌专家审核。

The elements of validation, as defined in this clause, are

本条款中规定的确认过程有:

a) IQ,

b) OQ, and

c) PQ.

In a health care facility, IQ and OQ are typically performed by the sterilizer manufacturer, although they can be performed by any qualified personnel. MPQ data might be available from the sterilizer manufacturer for general loads.

在医疗保健机构，IQ和OQ通常由灭菌柜制造商实施，当然，是由有经验的人员来实施。来自灭菌柜制造商的常用产品的MPQ数据可能是适当的。

For health care facilities, this means describing and documenting the following:

对医疗保健机构来说，意味着对下列事项进行说明和记录:

a) the validation steps that need to be performed;

需执行的确认步骤

b) the way in which these validation steps will be performed, along with a listing of responsible individuals, departments and/or outside contractors;

确认步骤执行的方法，责任人、责任部门和/或外部承包商名单;

c) the criteria for successful validation.

成功确认的准则。

For health care facilities, there is an option of contracting with an outside service to perform this validation; however, the health care facility is still responsible for ensuring that the validation complies

with the requirements of this International Standard.

对医疗保健机构来说，它可以选择由外部机构实施确认；但医疗保健机构仍然应对保证该确认符合本标准要求负责。

9.1.2 IQ is undertaken to demonstrate that the sterilization equipment and any ancillary items have been supplied and installed in accordance with their specification.

IQ是证明灭菌柜及其附件已按规范的要求安装完成。

9.1.3 OQ is undertaken to demonstrate the ability of the equipment to meet the performance requirements of its design specification.

OQ是证明灭菌柜的性能满足设计规范的性能要求；

9.1.4 PQ is the stage of validation that uses product to demonstrate that the equipment consistently operates in accordance with predetermined acceptance criteria and the process yields product that is sterile and meets the specified requirements.

PQ是使用产品的确认阶段，证明设备能持续按照预定的接收准则运行，灭菌过程能够使产品无菌，并满足规定的要求。

IQ and OQ may be a one-time exercise for the specific equipment being employed for a sterilization process. PQ should be carried out for each new process and/or product to be validated to demonstrate that the process complies with identified acceptance criteria and is capable of delivering the required SAL to the product.

对指定的用于灭菌过程的设备可以只实施一次IQ和OQ。每一个需确认的新产品和/或过程都应进行PQ，以证明灭菌过程符合规定的接收准则，及保证产品SAL的能力。

9.2 Installation qualification, IQ

9.2.1 Equipment设备

9.2.1.1 Equipment to be used in the sterilization process, including any

ancillary items, shall comply with its design specifications.

用于灭菌过程的设备，包括任何附件，应符合设计规范。

D.9.2.1.1 The supporting documentation for IQ should include descriptions of the physical and operational characteristics of the equipment (including ancillary equipment). Examples of relevant documents include design specifications, the original purchase order, user requirements specifications and functional design specifications.

IQ的支持性文件应包含设备的物理和操作特性描述。例如，相应的文件包括设计规范、采购订单、用户要求规范和功能设计规范。

The following are examples of equipment components that should be qualified to ensure that the equipment was installed according to the applicable specifications and requirements:

下面是必须合格的设备元件的举例，以确保按适用的规范和要求安装设备:

a) chamber and door construction;

柜室和门的结构;

b) seals and connections on chamber and piping construction (i.e. ability to maintain specified pressure and vacuum extremes);

灭菌柜室的密封和连接以及管道的结构 (如: 维持规定的压力和真空极值的能力);

c) supply systems for gases and liquids (e.g. air, nitrogen, steam, EO and water), including filters (if used);

气体和液体 (如:空气、氮气、蒸汽、EO 和水) 的供应系统 , 包括过滤器 (如使用);

d) the electrical supply, which should adequately and consistently supply the power needed for proper equipment and instrumentation operation;

供电系统，能为相应设备和仪器操作提供充裕、稳定和持续的电源;

e) gas circulation systems, where used; 气体循环系统，任何使用处

f) gas injection systems; 气体注入系统

g) vacuum systems, including pumps, pump cooling systems and piping;

真空系统，包括泵、泵冷却系统和管道;

h) exhaust, emission control and abatement systems;

排气、排放控制和减排系统;

i) other critical systems that could affect process conditions, such as process automation, safety systems, etc.;

可能影响过程状态的其它关键系统，如过程自动化系统、安全系统等

j) the calibration of instruments (e.g. sensors, recorders, gauges and test instruments) that monitor, control, indicate or record parameters such as temperature, humidity, pressure and EO concentration.

监视、控制、指示或记录参数(如温度、湿度、压力和EO浓度)的仪表的校验（如，传感器、记录仪、压力表和试验仪器）

k) the documented procedures for IQ should specify how each element of this qualification is planned, performed and reviewed.

文件化的IO程序应规定每一个验证元素是如何计划、执行和审核的。

9.2.1.2 Sterilization equipment shall comply with the applicable safety standards.

灭菌设备应符合适用的安全标准。

D.9.2.1.2 Guidance can be found in IEC 61010-2-40.

ICE 61010-2-40提供了指南。

9.2.1.3 The operating procedures for the equipment shall be specified. These operating procedures shall include, but are not limited to

应建立灭菌设备的操作规范。这些操作规范应包含，但不限于:

a) step-by-step operating instructions,

逐步的操作指导

b) fault conditions, the manner in which they are indicated, and actions to be taken,

故障条件，故障显示方式和处理措施；

c) instructions for maintenance and calibration, and

维护和校准说明，和

d) details of contacts for technical support.

技术支持联系人的详细信息。

9.2.2 Installation qualification

9.2.2.1 Installation of the equipment and all associated services shall be in accordance with the architectural and engineering drawings. The installation shall comply with all pertinent national, regional and local regulations.

设备的安装以及所有相关联的服务应符合构造和工程图纸的要求；安装应满足相关的国家、地区和地方法规的要求。

D.9.2.2.1 The location in which the equipment is to be installed should comply with all pertinent national, regional and local regulations.

设备安装的位置应符合全部相关的国家、地区和地方法规。

9.2.2.2 Instructions for installation shall be specified and shall include instructions pertinent to the health and safety of personnel.

应规定安装指南，安装指南应包含人员健康和安全的相关说明；

D.9.2.2.2 National and local requirements for occupational health and safety should be consulted as to how they apply to potential EO exposure.

要考虑国家和地方有关曝露于EO环境的职业安全与健康要求。

To protect the health and the safety of personnel, equipment that detects

atmospheric levels of EO or gas mixtures should be installed near the sterilizer and anywhere else where potential exposure could occur.

为保护人员健康和安全，在灭菌器附近及可能发生EO爆炸的任何其它地方应安装检测空气中的EO或混合气体含量的设备。

EO safety is achieved and maintained through a combination of factors that include:

达到和维持EO安全性的组合因素包括:

a) proper design, installation and maintenance of systems and equipment;

系统和设备的合理设计、安装和维护;

b) compliance with applicable regulations for occupational health and safety and for environmental protection;

遵守适用的职业健康和安全规范和环保规范;

c) development and implementation of policies and procedures that support safe work practices;

安全生产习惯的制度和程序的开发和执行

d) atmospheric monitoring in areas where EO exposure could occur;

任何可能发生EO曝露区域的大气监测

e) use of personal monitoring devices as appropriate;

适用时，使用个人监测装置

f) personnel training;人员培训

g) periodic audits of equipment, personnel and processes to ensure on-going compliance with design specifications and with the facility’s policies and procedures.

对设备、人员和工艺的定期审核，以保证始终符合设计规范和机构的政策和程序

In health care facilities IQ is generally the responsibility of the sterilizer

manufacturer, while in industrial facilities it is often performed by site personnel in conjunction with a factory representative. If the IQ is performed by the manufacturer, or by a third party, the facility is responsible for retention and management of documents and records relating to the purchase, installation of the equipment.

在医疗保健机构，IQ通常是灭菌柜制造商的责任，但在工业机构，通常由现场工作人员与厂方代表配合进行。如果IQ由制造商，或第三方进行，机构对与采购、设备安装相关的文件和记录的保存和管理负责。

9.2.2.3 Conditions for the safe storage of EO shall be specified to ensure that its quality and composition remain within specification.

应规定EO贮存的条件，以确保EO的质量和组分保持在规范要求内。

D.9.2.2.3 The storage conditions for EO should be in accordance with the EO manufacturer's recommendations and all applicable regulations.

EO贮存条件应满足EO制造商推荐和全部适用的法规要求。

9.2.2.4 Prior to IQ, the calibration status of any test instrumentation used during the IQ shall be confirmed.

实施IQ前，应确认在IQ期间使用的任何试验仪表的校准状态。

9.2.2.5 Drawings of the equipment as installed, plumbing and other ancillary equipment shall be finalized during IQ.

IQ期间，安装设备的、水暖及其附属设备的图纸应已完成

D.9.2.2.5 Drawings, process and instrumentation diagrams (P&ID), and schematics should be checked against the as-installed configuration and updated where necessary.

应对照图纸、工艺仪表图(P&ID)电路图检查已安装的结构，必要时进行更新。

Drawings and parts lists for the equipment should include:

设备图纸和部件清单应包括：

a) pipe work and instrumentation schematic drawings (i.e. process and instrumentation diagrams);

管道工程和仪表电路图 (如，安装流程图)；

b) a list of other pertinent mechanical and electrical drawings and their location;

其它相关的机械和电气图纸及机械-电气位置清单；

c) a list of critical instruments and devices, particularly those influencing process control, for which physical characteristics and manufacturer performance claims (e.g. accuracy, repeatability, size and model) should be kept on file;

关键仪表和装置清单，特别是那些会影响过程控制的仪表和装置；档案中应保存这些仪表和装置的物理特征和制造商有关仪表和装置性能 (如精确度、可再现性、规格、型号等) 的文件；

d) process control logic or software documentation necessary to support validation, including control system layout, control logic diagrams and application software (computerized measurement and control systems) such as program listings, flow charts, ladder logic diagrams where applicable and strategy diagrams.

支持确认所必需的过程控制逻辑或软件文件，包括控制系统布局、控制逻辑图和应用软件 (计算机化测量和控制系统)，如程序列表、流程图、 梯形逻辑图 (如适用)，策略图。

9.2.2.6 Changes made to systems during the IQ shall be assessed for their impact on the design and process specification and documented in the design history file.

IQ期间，应评估系统变更对设计和过程规范的影响，并记录在设计历史文档中。

9.3 Operational qualification, OQ

9.3.1 Prior to OQ, the calibration of all instrumentation (including any test

instruments) used for monitoring, controlling, indicating or recording of the sterilization process shall be confirmed (see 4.3.3).

在OQ之前，应对用于灭菌过程监视、控制、指示或记录的所有仪表(包括任何试验仪器)进行校准。

D.9.3.1 The following information should be documented for all instrumentation used for monitoring, controlling, indicating or recording:

应记录用于监测、控制、指示或记录的所有仪表的下列信息

a) equipment identification;设备身份标识

b) calibration schedule;校验计划

c) actual completion date for each calibration, as well as who performed it;每一次校准完成的实际日期，及校准执行人

d) the next scheduled calibration date.下一次计划校准日期

9.3.2 OQ shall demonstrate that the installed equipment is capable of meeting its operating specification.

OQ应证明安装的设备能满足其操作规范的能力

D.9.3.2 OQ for EO equipment is carried out either with an empty sterilizer chamber or using appropriate test material to demonstrate the capability of the equipment to deliver the range of operating parameters and operating limits contained in the process specification. This range of parameters and operating limits should include the initial sterilization process that has been defined in process definition (see Clause 8).

可使用空的灭菌柜或用适当的试验材料来实施EO设备的OQ，以证明设备在操作参数范围内运行的能力和在包含过程规范的操作极限下运行的能力。这一系列操作参数和运行极限范围应包括在过程定义中已规定的初始灭菌工艺 (见条款 8)。

OQ should also determine the performance of associated ancillary systems. For example, the capability of the EO vaporizer to achieve a minimum EO input

temperature.

OQ应确定相关的辅助系统的性能。如，EO汽化器在低温度下汽化EO的能力。

The system software (e.g. computerized measurement and control systems) should be tested in all fault conditions during OQ. The user is responsible for assuring the software is validated.

OQ期间，应在所有故障条件对系统软件(如，计算机测量和控制系统)进行试验。判定软件已被确认是使用者的责任。

OQ can include the following when using a predefined cycle:

当采用预定的周期时，OQ可能包括下列:

a) Preconditioning Phase 预处理阶段

1) The pattern of air circulation throughout the area to be occupied by the sterilization load(s) should be determined. This can be performed by smoke tests in combination with calculation of air change rates and anemometric determinations.

应确定放有灭菌产品(装载)的整个预处理区的空气循环模式。这可以通过与空气变化率的计算和风力测定相结合的烟雾测试来进行。

2) Temperature and humidity should be monitored throughout the preconditioning area over a period long enough to demonstrate that values are maintained within the desired ranges. The temperature and humidity in a number of locations distributed throughout the preconditioning

area should be determined.

应通过一个足够长的周期监视整个预处理区的温度和湿度，以证明温度和湿度能保持在规定的范围内。应测定整个预处理区多个位置的温度和湿度。

NOTE See Table C.1 and Table C.2 for recommendations on the number of temperature and humidity sensors.

注，推荐的温度和湿度传感器的数量内见表C.1和表C.2

b) Sterilization Phase 灭菌阶段

1) If inert gases are used instead of EO, account should be taken of the differences in the relative heat capacity when assessing the results.

如果惰性气体代替EO进行OQ运行时，当评估结果时应陈述在相应的热容量的不同处。

2) Temperature/humidity distribution: Temperature/humidity sensors should be located in those locations that are likely to represent the maximum temperature differential, such as locations near unheated portions of the chamber or door and locations near steam or gas entry ports. The remaining temperature sensors should be distributed evenly throughout the usable chamber volume.

温度和湿度的描述:温度/湿度传感器应放置在能代表最大温度差异的位置，如靠近未加热的柜或门的部位，或靠近蒸汽或气体进入部件的位置。应将温度传感器均匀分布在可用柜室体积内。

NOTE See Table C.1 for the recommended number of sensors.

注，推荐的传感器的数量内见表C.1和表C.2

3) In empty chamber OQ exercises, the recorded temperature range, within the usable chamber volume during EO or inert gas exposure, of ± 3 ° C of the average recorded chamber temperature at each time point should be obtained after an equilibration period. When the OQ exercise is carried out using a loaded chamber, then the ± 3 ° C tolerance might not be achievable.

OQ在空柜下进行时，在一个平衡的周期后，记录的温度范围，在EO或惰性气体暴露的情况下，每一个时间点的记录的柜室温度的平均偏差不超过± 3 ° C。当OQ在装载状况下实施时，± 3 ° C的公差可以不达到。

4) chamber leak rate (performed either under vacuum for subatmospheric cycles or under vacuum and at pressure for superatmospheric cycles);

柜室泄漏率[进行正压或负压周期]

5) pressure rise on injection of steam during the conditioning phase;

处理阶段蒸汽注入时的压力上升;

6) the temperature of the injected EO-gas should be within the volatizer specification or above the boiling point of EO (10,7° C at atmospheric pressure);

EO气体注入温度应在汽化器规范内或高于EO沸点(10.7℃，大气压下)

7) pressure rise and rate of attainment on admission of EO and correlation of factors with which it is intended to monitor EO concentration;

EO导入的速率和压力升高，以及与监测浓度有关的因素的收集。

8) depth and rate of attainment of vacuum used to remove EO;

用于去除EO的真空度和真空速率;

9) pressure rise and rate of attainment of pressure on admission of air (or other gases);

空气(或其他气体)导入时的压力速率和压力升高。

10) number of times these last two stages are repeated and any variations in successive repetitions;

最后二个阶段的重复次数和连续重复时的任何变化。

11) the reliability of the supply of filtered air, inert gasses, water and steam;

提供过滤空气、惰性气体、水和蒸汽的可靠性;

12) replicate cycles should be carried out to demonstrate the repeatability of control;

应实施重复周期，以证明控制的重现性

13) a chamber wall temperature study should be completed to verify adequate

temperature uniformity provided by the jacket heating system. The study should characterize the temperature profile for comparison on a periodic basis to ensure the system continues to operate effectively.

应完成柜壁温度的研究，以证明通过夹层加热系统加热的充分的温度均匀性。

这个研究应表征温度定期比较的趋势，以确保加热系统有效地持续运行

c) Aeration Phase通风阶段

1) When performing aeration, the temperature profile of the aeration area should be determined in the same manner as recommended for preconditioning areas. The air flow rates and air flow patterns through the area should also be determined.

当进行通风处理时，与推荐给预处理一样的方式，测定通风区的温度趋势。应确定整个通风区的空气流动率和空气流动模式。

9.4 Performance qualification, PQ

9.4.1 General

D.9.4.1 PQ consists of rigorous microbiological and physical testing, beyond routine monitoring, to demonstrate the efficacy and reproducibility of the sterilization process. PQ is normally not started until after completion and approval of the IQ and OQ testing. Acceptance criteria should include conformance with the specifications for the sterilization process parameters and microbiological challenge. PQ activities should be clearly defined in a written document (e.g. protocol). Where elements of the PQ are carried out by separate parties, those parties should approve the relevant documentation. See 4.1 and 4.2.

PQ 由严格的微生物试验和物理试验构成，在超越日常监视的条件下，来证明灭菌过程的有效性和重现性。在IQ和OQ完成和批准前，通常不进行PQ。接受准则应包括灭菌过程参数规范与微生物挑战的一致性。PQ活动应清楚地在完成的文件(如,方案)定义。不管PQ的元素在哪里被分隔进行，均应批准相应的文件。

9.4.1.1 PQ consists of both microbiological and physical performance qualification and is performed in the equipment used to sterilize the product.

PQ由微生物性能和物理性能验证组成，并在用于灭菌该产品的设备中进行。

9.4.1.2 PQ shall be performed on the introduction of new or modified products, packaging, load configuration, equipment or process parameters, unless equivalence to a previously validated product, packaging, load configuration, equipment or process has been documented. (See 7.1.2, 7.1.6 and 12.5.)

引入新的或改造过的产品、包装、装载方式、设备或过程参数时，应进行性能鉴定，除非与预先已经验证的产品、包装、装载方式、设备或过程的等效性已经记录。（见7.1.2,7.1.6和12.5)

9.4.1.3 PQ shall use product, or material representative of that to be sterilized routinely, to demonstrate that the equipment consistently operates in accordance with acceptance criteria and that the process produces product that meets the intended SAL.

PQ应使用有代表性的产品或材料，以证明设备的持续运行符合接收准则及过程产品满足预定的SAL要求。

9.4.1.4 The manner of presenting product for sterilization, including the load configuration of a product, shall be specified.

应规定灭菌过程的产品提供形式，包括产品的装载方式

NOTE If saleable product has been used during validation, 7.2 provides information concerning the product quality for patient use and 11.4 provides information concerning the requirements for the release of sterile product.

如果确认时使用是可销售的产品，7.2条款提供了涉及给患者使用的产品质量的信息,11.4条款提供了涉及无菌产品放行的设备的信息

D.9.4.1.4 In specifying the presentation of product, both load configuration (the composition of the load) and the placement of items within the load should be considered.

在规定的产品介绍中，应考虑装载方式和装载中的产品放置。

Typical load parameters to be defined might include stacking configuration, overall density, dimensions, material composition, and use and type of pallet wrap. Load configuration should be documented for each sterilizer. If routine sterilization consists of product loads that are less than the full chamber, then the MPQ/PPQ should incorporate the minimum load.

定义的装载参数可以包括堆叠方式、总体密度、尺寸、材料组成和使用的托盘的类型；每一灭菌柜的装载方式均应文件化。如果日常灭菌由比满柜少的产品装载组成，那么，MPQ/PPQ应包括最小装载。

Product placement should also be specified. In a large industrial sterilizer, this would refer to the positioning of cases in a pallet or tote. For smaller sterilizers, as used by health care facilities, this refers to the positioning of baskets, packs and rigid containers on a sterilization carriage or carrier.

应定义产品的放置方法。在较大的工业灭菌柜中，这将为托盘或搬运箱中外箱的位置提供参考。对于相似的灭菌柜，由医疗保健机构使用时，这将为托盘或搬运箱中外箱的位置提供参考。

The product and load used during PQ should be at least as difficult to sterilize as the most challenging load expected during normal production. The load can consist of product or materials that have characteristics similar to those of a load to be sterilized routinely. Changes in the load configuration can affect the lethality of a sterilization process. It is important that the acceptable load configurations be specified. If multiple load configurations are allowed, the load configuration used in the PQ studies should represent the most difficult-to-sterilize configuration, or should have a known relationship to the most difficult-to-sterilize configuration. Some variations in the load size might be justified as having no significant impact.

用于PQ的产品和装载应至少与计划用于常规生产的最大挑战的装载具有同样的最难灭菌。装载可以由产品或与灭菌产品特性相似的材料组成。装载方式的任何变化都可

能影响灭菌过程的杀死力。装载方式的规定是十分重要的。如果允许多种装载方式，那么，用于PQ研究的装载方式应能代表最难灭菌方式，或应具有与已知的最难灭菌装载方式的关联性。装载方式的一些变化，如没有明显的影响，是可能接受的。

During PQ, two types of load can be chosen:PQ时，二种装载类型可以选择

a) saleable product;

可销售产品

b) non saleable product or appropriate test material.

不可销售产品或适当的试验材料。

9.4.1.5 The load used for PQ shall be representative of that to be sterilized routinely and shall be defined based upon the most challenging routine load.

用于PQ的装载应具有代表性的，且是最具挑战的日常装载。

D.9.4.1.5 When the load is composed of products, such as surgical kits, lumens of varying size and length, various packaging, and varying physical mass that contain a number of different materials (e.g. plastics, metals, cotton, etc.), it is important to verify the load configuration because these materials might not behave similarly when heated during preconditioning and conditioning.

当装载由产品组成时，如外科包、各种形状和长度的管子、各种包装和各种包含许多不同材料的物理物块(如，塑料、金属、棉花等)，当在预处理和处理的加热过程时，由于这些材料没有相似的表现，证明这些方式是十分重要的。

9.4.1.6 For establishments that have widely varying load configurations, the extent to which the variation affects the sterilization process shall be evaluated. It shall be demonstrated that all product exposed to a sterilization process achieves the required SAL.

对于各种装载方式，应评估装载方式的变化对灭菌过程的影响程度；应证明经灭菌的产品能达到规定的SAL.

D.9.4.1.6 In addition to considering maximum/minimum load size (see D.9.4.1.4)

and product effects (see D.9.4.1.5), validation load composition should consider any widely varying load material/packaging characteristics routinely sterilized, when developing a representative or most challenging load for validation.

附加考虑最大/最小装载形状(见D.9.4.1.4)和产品影响，当开发一个用于确认的有代表性的或最具挑战的装载时，确认用的装载组合应考虑用于常规灭菌的广泛的各种装载材料/包装的特性。

Products or surrogate product materials utilized in validation loads should represent those that typically present the most challenging condition for lethality (i.e. for penetration of heat, humidity, and EO gas diffusion; density). Consideration should be given to include load material with substantially varying characteristics such as: absorbent materials, barriers to diffusion such as rigid materials, sealed liquids, containers, etc.

产品或替代产品材料用于确认的装载应代表那些通常提供对杀死力而言最具挑战条件的(如，针对热、湿的渗透，EO气体的扩散；密度).包括特性差异大的材料如吸水性材料，妨碍扩散如坚硬材料，封口的液体、容器等。

9.4.1.7 If material other than product is used, it shall present at least as great a challenge to the sterilization process as the product.

如果使用产品外的其他材料，应证明该材料对灭菌过程挑战性至少与产品一样。

9.4.1.8 If loads are reused for the validation cycles, they shall be aerated between exposures to meet the regulations for worker safety and to ensure that EO residues in the load do not affect the biological challenge in the next microbiological PQ study.

如果装载被重复使用于确认周期，装载应通风，直到满足针对工人安全的法规，并确保装载中的EO残留在接下来的微生物PQ研究中不会影响微生物挑战性。

D.9.4.1.8 If the load is to be re-used during PQ, the loads should be aerated and re-equilibrated to ambient conditions prior to starting the next run. After repeated use, the suitability of the load should be considered. Aeration

between exposures will ensure that EO residues in the load do not affect the biological indicator. If equilibration time is insufficient, the load could be warmer than the normal ambient conditions, or the load humidity could be much lower than the normal ambient load conditions. Either of these situations produce data that are not representative of normal production. Too high a starting temperature produces an unrealistically rapid kill rate. Too low a humidity, where test spores become desiccated, produces an unrealistically low kill rate. Also, too high a humidity that results in an environment condition where the environmental dew point is higher than the product and/or load temperature results in condensate formation in the load and product that results in a low and erratic kill rate.

如果PQ时重复使用装载，那么，在用于下一个周期前，装载应通风和与环境条件再平衡。二次暴露间的通风，将确保装载中的EO残留不会影响BI。如果平衡时间不充足，装载就会比环境条件热，或装载的湿度比环境条件低。这二种状况都能产生不能代表日常生产的数据；一个太高的开始温度产生虚高的快速杀灭率。太低湿度，试验孢子变成干燥的，产生一个不真实的低的杀死率。当然，湿度太高，当环境露点高于产品的温度时，可能导致产品和/或装载上冷凝水的存在而导致杀灭效果的降低与不确定。

9.4.1.9 If chemical indicators are used as part of PQ, these shall comply with ISO 11140-1, and shall be used in conjunction with microbiological and physical monitoring.

如果PQ使用了化学指示剂，化学指示剂应符合ISO11140-1，应结合微生物和物理监视使用。

9.4.1.10 Biological indicators used in PQ shall comply with the applicable clauses of ISO 11138-1:2006 and ISO 11138-2:2009, Clause 5 and 9.5.

用于PQ的生物指示剂应符合ISO11138-1:2006和平ISO11138-2:2009标准5和9.5的要求。

9.4.2 Performance qualification — Microbiological PQ——微生物

9.4.2.1 The microbiological PQ (MPQ) shall demonstrate that, on application

of the sterilization process, the specified requirements for sterility are met. Studies shall be performed in the production chamber using defined process parameters selected to deliver less lethality than the specified sterilization process.

微生物性能验证(MPQ)应证明灭菌过程的运行能满足规定的灭菌状态的要求。研究应在生产柜室内进行，所选的微生物杀死力的过程参数应低于定义的灭菌过程参数。

D.9.4.2.1 Results obtained during process definition and, where applicable, IQ and OQ should be used to set the parameters for MPQ. Exposure time is the key parameter that is varied during microbiological qualification. Other parameters can be adjusted as necessary to provide assurance that the MPQ delivers less lethality than the normal production process. For example, temperature, humidity, and/or EO concentrations could be run at set points that are at the lower extreme of the normal process range. This would provide assurance that any observed values within the specified range will produce acceptable lethality.

应根据IQ和OQ定义的运行结果设定MPQ的参数。对于MPQ来说，暴露时间是十分重要的。为提供MPQ低于日常生产过程杀死力的证明，可以调整其他的参数。如，湿度、湿度和/或EO浓度可以设定在日常过程参数的下限。这将证明参数在规定范围内都可以产生可接受的杀死力。

MPQ should be conducted using product that is at or below the minimum temperature specified for product to enter the preconditioning area. If it is anticipated that initial product temperature could vary, for example because of transport for sterilization at a remote facility, the design of the qualification testing should reflect this possibility.

MPQ使用的产品，其温度应等于或低于规定的进入预处理区的产品最低温度。例如，边远工厂的产品运输，验证试验的设计会产生这个可能。

For fractional cycles (sub-lethal or half cycle), it might also be necessary to shorten the post-exposure phases of the cycle or to remove BIs prior to

the aeration phase or after an abbreviated aeration phase. This is done to minimize “residual kill” of the BIs due to EO that is present in the load during the aeration phases of the cycle. When shortening the post-exposure phases of the cycle, factors such as operator safety should be taken into account. The parameters selected for MPQ, with the exception of exposure time, should remain fixed throughout MPQ.

对短周期(低杀死力或半周期)来说，需要缩短周期的后暴露阶段或，在通风阶段前或短时的通风阶段后取出BI。这可使通风阶段装载内的残留EO对BI的‘剩余杀死力’减到最少。当进行这种操作时应考虑操作人员的安全性。包含异常的暴露时间的MPQ运行参数，在MPQ过程中保持不变。

NOTE Attention is drawn to the existence of statutory regulations existing in some countries on personnel exposure to EO.

注，应注意有些国家有关暴露于EO的操作人员的现有法规。

9.4.2.2 MPQ shall confirm the effectiveness of the defined process for the product/load combination in a production chamber.

微生物学性能鉴定应确定针对在生产柜室内的产品/装载组合的定义过程的有效性。

D.9.4.2.2 The microbiological challenge defined in MPQ should be designed to ensure the required SAL is attained for all product load combinations. To achieve this objective, it is common to use PCDs or a worst case product to represent EO product families.

MPQ定义的微生物挑战的设计，应确保所有的产品装载组合都能到达规定的SAL。为达到这个目的，通常使用PCD或最坏包装产品来代表EO产品族。

PCDs should be placed within the product case and evenly distributed in the sterilization load, but distribution should include those locations where sterilization conditions are the most difficult to achieve. The locations used should include those selected for temperature monitoring. For loads that are palletized, these locations should also include the top and bottom of the pallets to ensure that all potential stratification within the chamber is

assessed.

PCD应放置于产品盒内或分布于灭菌装载内，但分布应包括那些灭菌条件最难到达的位置。这些位置应包括那些温度监视点。对于用托盘的装载，这些位置应包含这托的顶部和底部，以确保灭菌柜内的所有的可能的分层得到评估。

For guidance on sample numbers, see Table C.3.

有关样本数量的指南，见表C.3

9.4.2.3 The lethality of the cycle shall be determined using one of the methods described in Annex A or Annex B or by an alternative method that demonstrates achievement of the required product SAL.

使用附录A或附录B描述的方法之一或用可替代的方法，来测定周期的杀伤力，证明规定的产品SAL的达到。

9.4.2.4 If process definition was determined in a developmental chamber, the MPQ shall include at least three fractional or three half cycles in the production chamber that confirm the data from the developmental chamber.

如果过程定义是在开发柜室中确定的，那么，在生产柜室中至少应进行三次短周期或三次半周期的MPQ，以验证来自研发性灭菌柜的数据。

D.9.4.2.4 If a developmental chamber was used for process definition, consideration should be given to establishing the relationship between data from the developmental chamber studies and data from the production chamber. The development of the microbial inactivation curves is not always possible in production chambers because of the size of the chamber and the time required to inject and remove EO in the chamber. These long injection and vacuum times limit the ability to obtain the required fractional recovery of indicator organisms. These inactivation curves can be developed in a developmental chamber that can deliver equivalent parameters especially EO concentration used in the production chamber. Methods for demonstrating a relationship between the data developed in the developmental chamber and a production chamber involve a physical profile comparison and load density comparison.

The sterilization conditions delivered in the developmental chamber should be compared with the physical profile obtained in a production chamber. Comparison of the lethality obtained in the development chamber and production chamber should take into account the differences in EO gas injection and evacuation times of the two chambers.

如果过程定义使用的是研发性柜室，应考虑规定研发性柜室研究的数据与生产性柜室的数据的关联性。由于柜室的型号和规定的注射和去除柜内EO的时间原因，并不是所有微生物存活曲线都可以在生产性柜室中进行；较长的注射和真空时间，限制了获得规定的短时的指示生物的复活的能力。这些存活曲线能在研发性柜室内开发，研发性柜室的参数尤其是EO浓度应与生产性柜室等同。证明研发性柜室的开发数据与生产性柜室之间的关联性的方法包括一个外观(物理轮廓)比较和装载密度比较。研发性柜室中获得的灭菌条件应与生产性柜室中获得的物理轮廓比较；研发性柜室获得的杀死力和生产性柜室的比较应记录二种柜室间的EO注射和抽真空时间的差异

During the development of the sterilization process in a developmental chamber, it is important to place PCDs inside the finished product case or in the routine configuration to provide a relationship of the dynamics of the products within the case against the PCD during process development.

在研发性柜室的灭菌过程开发期间，将PCD放入完成的产品箱内或日常装载方式内，以提供在过程开发期间箱内产品与PCD的动态关联性。

9.4.2.5 If the overkill half cycle approach [see B.1.2 a)] is used, then there shall be no positive internal PCDs from the half cycle runs.

如果采用半周期过度杀灭法(见B.1.2)，那么，半周期运行中应无阳性的内部PCD.

Positive external PCDs during the half cycle are acceptable if they have demonstrated greater resistance than the internal PCDs providing a “worst-case challenge” for routine processing. However, all internal PCDs should test negative.

如果已经证明用于日常加工的外部PCD比提供‘最坏状况挑战’的内部PCD有更大的抵抗力，半周期时出现阳性的外部PCD是可以接受的。否则，内部PCD应是全部阴性的。

9.4.2.6 If the overkill cycle calculation approach [see B.1.2 b)] or the BI/bioburden approach (see Annex A) is used, there may be some surviving internal PCDs, but the calculated SAL shall meet the specified value (See ISO 14161).

如果采用过度杀灭周期计算法(见b.1.2)或BI/生物负载法(见附录A)，允许有存活的内部PCD存在,但计算得出的SAL应满足规定值(见ISO14161)。

9.4.3 Performance qualification — Physical 性能验证——物理

9.4.3 NOTE Results obtained from OQ can be used to identify features needing evaluation during PPQ.

注，OQ中获得的结果可用于识别PPQ需要评估的特性。

9.4.3.1 Physical PQ (PPQ) shall demonstrate

PPQ应证明:

a) that the specified acceptance criteria are met throughout the load for the duration of the proposed routine process specification, and

经过常规加工规范灭菌的任何装载能满足规定的接收准则。

b) reproducibility of the process.

过程再现性

The PPQ shall include a minimum of three planned qualification cycles, consecutive in the same study, in which all the specified acceptance criteria are met. PPQ may be conducted during the MPQ. If PPQ is performed in parallel with at least three MPQ runs, then a minimum of one additional PPQ run shall be performed using the full routine process specification.

至少进行三次连续的同样的PPQ,且均应满足规定的接收准则。PPQ可以在MPQ期间进行。如果PPQ与至少三次MPQ运行结合进行，那么，应至少增加一次全灭菌过程用于PPQ运行。

If a failure can be attributed to factors not relevant to the effectiveness

of the process being validated, this may be documented as unrelated to the performance of the process without requiring three further consecutive successful runs. Examples of this type of failure may include, but are not limited to, power failures, other loss of services, or failure of external monitoring equipment.

如果失效的原因与验证过程的有效性因素无关，则可记录为与过程性能无关，不需要再进行连续三次成功的运行。此类失效类型包括但不限于电力中断、其它服务的缺失、或外部监视设备失效。

D.9.4.3.1 If, in any of these runs, sterility or product functionality requirements are not met, an investigation should be conducted to determine if additional qualification runs are necessary. If process parameters cannot be maintained within the defined limits, an investigation should be conducted. If modifications are made, additional runs might be necessary.

如果，这些周期的任何一次，无菌或产品功能要求未满足，要进行一次调查以证明是否需要增加一次验证。如果过程参数不能保持在规定的限度内，应进行调查。如要改进，可能需增加运行。

9.4.3.2 PPQ shall confirm the process such that:

PPQ应确认如下过程:

D.9.4.3.2 PPQ should be carried out with the loading patterns and pallet separations specified in the documented procedures. For large preconditioning areas where a small load will not have a significant effect on the area dynamics, it is not necessary (and indeed might be impractical) to perform the studies with the preconditioning area in various loading states.

PPQ应用文件化的规定的装载模式和托盘进行；对于较大的预处理室内的小的装载，在区域动力学方面不会有显著的影响，没有必要进行预处理区各种装载状态的研究。

The guidance on PPQ of preconditioning also applies to the performance qualification of conditioning (i.e. during sterilization). See Table C.1 and Table C.2 for the recommended minimum number of sensors.

关于预处理PPQ的指南，同样适用于处理的性能验证。建议的最少传感器数见表C.1和表C.2。

a) the minimum temperature of product to enter the sterilization process and/or the defined conditions required to achieve it shall be established;

应建立进入灭菌过程的产品的最低温度和/或要求达到的规定条件。

b) at the end of the defined preconditioning time (if used), the sterilization load temperature and humidity have been established;

在规定的预处理(如使用)时间结束时，灭菌产品的温度和湿度应在规定范围内。

b) It is important to establish and report the product temperature and humidity ranges of the sterilization load after exposure to the specified preconditioning time (if used).

规定和报告暴露于规定的预处理时间(若采用)后的灭菌产品(装载)的产品温度和湿度范围是十分重要的。

c) the specified maximum elapsed time between the completion of preconditioning (if used) and the commencement of the sterilization cycle is appropriate;

从预处理(若采用)完成到灭菌周期开始之间规定的最大的消耗时间是适当的。

c) During the product transfer from preconditioning (if used) to the sterilization chamber, conditions of product temperature and humidity might be impacted. It is important to ensure that this effect is considered during PQ and is commonly addressed during PQ by ensuring that the time of transfer specified in the PQ reflects the maximum time specification to be used for product transfer during routine sterilization.

产品从预处理转移到灭菌柜期间，产品温度和湿度的条件可能受影响。应能保证PQ中规定的转移时间能反映在日常灭菌时用于产品转移的最长时间规范。

d) at the end of the defined conditioning time, if used, the sterilization load temperature and humidity have been established;

在设定的处理时间结束时,若采用，灭菌物品的温度和湿度应在规定的范围内;

d) Temperature and humidity sensors should be located within the sterile barrier system or amongst the unit packages in the sterilization load. When preconditioning is used, the product should be preconditioned within the specified time range. When preconditioning is not used, the temperature and relative humidity within the load should be within defined limits prior to the end of the conditioning phase of the cycle.

温度和湿度传感器应放置在灭菌产品(装截)中无菌屏障系统内或单位包装中。当采用预处理时，产品应在规定的时间范围内进行预处理。当不采用预处理时，灭菌周期的处理结束前，装载内的温度和相对湿度应在规定的限度内。

The temperature and humidity profile within the sterilization load should be evaluated during the time that is needed for the sterilization load to attain the minimum predetermined temperature and humidity.

应评估在灭菌产品达到预定的最小温度和湿度所需的时间期间内，灭菌产品(装载)内的温度和湿度的趋势。

For product, consideration should be given to locating humidity sensors in areas of the load that are most likely to experience variation in humidity, e.g. pallet centers, pallet edges and surfaces. For PQ, humidity sensors should be placed within the packaging (where possible) within the load. This can be achieved by placing the sensor within the sterile barrier system or amongst the unit packages.

对产品来说，应考虑到，将湿度传感器放置在最能体现湿度变化的装载区域内，如，托盘的中心、托盘边缘和表面。对于PQ，温度传感器应放置在装载内包装内。可以通过把传感器放置在无菌屏障系统或单位包装内来实现。

e) the chamber humidity was recorded if parametric release was to be used;

如果采用参数放行，应记录柜室的湿度;

f) gaseous EO has been admitted to the sterilizer chamber;

EO气体已进行灭菌柜室

f) If parametric release is used, the EO concentration profile for the entire gas dwell phase should be assessed to determine how the gas concentration changes over the phase.

如果采用参数放行，应评估整个气体保持阶段的EO浓度状态，以确定这个阶段的气体浓度变化。

g) pressure rise and the quantity of EO used or concentration of EO in the sterilizer chamber have been established [see 9.5.4 f)]. If parametric release is to be used, also see 9.5.5 b);

灭菌柜室的压力升高、EO重量或EO浓度（见9.5.4f)在规定的范围内。如采用参数放行，见9.5.5 b);

h) during the sterilization cycle, the temperature and humidity (if recorded) of the chamber and, where applicable, other process parameters have been established;

在灭菌周期时，灭菌柜的温度和湿度（若记录）和其它适用的过程参数在规定的范围内;

i) the temperature of the product load during exposure has been established;

在EO暴露期间产品装载的温度在规定范围内。

i) The temperature sensors within the sterilization load should be placed in the locations that are most likely to experience the greatest temperature variation. These locations should take into account hot or cold spots located during OQ. The locations of hot and cold spots within a load can be significantly different than the locations in an empty chamber.

灭菌产品内的温度传感器应放置在最能体现最大温度变化的部位。这些部位应考虑到OQ时的冷点和热点。装载内冷点和热点的部位可能与空柜的部位明显不同。

During PQ, it is important to take into account the relationship between the load temperature and the chamber temperature in order to ensure adequate load

temperature in the routine process. If sensors are used in the sterilization chamber and 100 % EO or potentially flammable sterilant mixtures are used, the temperature and humidity sensors should be intrinsically safe, or should be of an explosion proof design. These sensors should also be functionally compatible with EO and with any diluent gases.

在PQa期间，为确定在日常过程中的充足的装载温度，应考虑到装载温度和柜室温度间的关联。在灭菌柜和100%EO或潜在的可燃灭菌剂混合物中使用传感器，温度和湿度传感器应是安全的，或应具有防爆设计。这些传感器应具有与EO和任何稀释气体兼容的功能。

j) during aeration (if used), the temperature of the sterilization load has been established.

在通风期间(若使用)，灭菌产品的温度在规定范围内。

j) The temperature within the sterilization load during the aeration process should be measured over the period of time required for the sterilization load to attain acceptable residual levels or measured over the period of time required for the sterilization load temperature to stabilize.

NOTE This can be established during additional studies after completion of MPQ/PPQ.

应测定在通风过程期间规定的整个时间范围内的灭菌产品内的达到可接受的残留水平的温度，或测定整个时间周期内的要求的稳定的灭菌产品的温度。

9.5 Review and approval of validation确认的审核和批准

9.5.1 The purpose of this activity is to undertake and document a review of the validation data to confirm the acceptability against the approved validation procedures/protocol for the sterilization process and to approve the process specification.

此项活动的目的是实施与记录确认数据的审核，以证实针对经批准的灭菌程序/方案的可接受性，并对过程规范进行批准。

9.5.2 Information gathered or produced during product definition, process definition, IQ, OQ and PQ, including results from incubation of biological indicators, shall be recorded and reviewed for acceptability. The results of this review shall be recorded.

在产品定义、过程定义、IQ、OQ和PQ过程中收集或产生的资料，包括生物指示物的培养结果，应予以记录并审核其可接受性（另见4.1.2）。应记录审核的结果。

D.9.5.2 Any discrepancies observed during the validation process should be documented, and their effect on the results of the validation should be determined and documented.

应记录在确认过程期间观察到的差异，以及确定和记录对确认结果的影响。

9.5.3 A validation report shall be prepared. The report shall be reviewed and approved by the designated responsible person(s).

应编制确认报告。报告应由指定的负责人进行审核与批准。

D.9.5.3 Typically the validation report is approved by the designated responsible person(s) as defined in the validation protocol.

通常情况下，确认报告由在确认方案中规定的特定的负责人。

9.5.4 The validation report shall describe or reference specific qualified product, defined load configurations and the documented specification for the EO sterilization process and shall address:

确认报告应描述或引用指定的合格产品，定义的装载方式和形成文件的EO灭菌过程规范，并应表明：

NOTE For practical purposes, rates can be determined as the time taken (with tolerances) to attain a specified pressure change.

注，当达到规定压力所需的时间变化时，说明变化的速率。

a) the minimum temperature of product to enter the sterilization process and/or the defined conditions required to achieve the minimum required

temperature;

产品进入灭菌过程的最低温度和/或达到要求的最低温度的定义的条件

b) preconditioning (if used):预处理:

1) time in chamber/area, temperature and humidity of chamber/area;

柜室/区内的时间、温度和湿度

2) temperature and humidity of the sterilization load;

灭菌产品的温度和湿度

3) maximum elapsed time between removal of the load from preconditioning and commencement of the sterilization cycle;

装载从预处理转移到灭菌周期开始的最大所需时间

c) vacuum levels and rate of evacuation (if used):

真空水平和真空速率

1) holding time under vacuum (if used);

真空保持时间

NOTE The rate of evacuation is commonly specified as either a minimum allowed evacuation time, a maximum allowed evacuation time or as an acceptable range of evacuation times, rather than the specific time for each run.

注，当最低真空时间、最大真空时间或当真空次数的范围，相当于每次运行的规定时间时，要规定真空的速率。

d) inert gas flushing (if used):惰性气体清洗(如使用)

1) pressure (ΔP or terminal pressure) and rate (ΔP/time) of attainment of pressure associated with inert gas/steam;

压力(ΔP或终端压力)和与惰性气体/蒸汽相关的压力变化速率。

2) depth (ΔP or terminal pressure) and rate (ΔP/time) of attainment of vacuum;

深度和真空速率

3) number of times of repetition and any variations in successive repetitions;

重复的次数和各次间的变化;

e) conditioning and/or humidity dwell phases (if used):

处理和/或湿度保持阶段(如采用)

1) pressure levels and/or rate of attainment of vacuum or relative humidity levels (whichever is being controlled and monitored);

压力水平和/或真空速率或相对湿度水平(需控制和监视)

2) number of steam pulses/vacuum (if used);加蒸汽/抽出的次数

3) time;时间

4) chamber temperature;柜室温度

5) temperature and humidity of the sterilization load at the end of conditioning;处理结束时的灭菌产品的温度和湿度。

f) EO injection and exposure:EO注射和暴露

1) EO injection pressure rise (ΔP), EO injection time and terminal pressure of EO injection phase;

EO注射压力升高, EO注射时间和EO注射结束时的压力

2) evidence that the gaseous EO has been admitted to the sterilization chamber by the pressure rise and by one of the following;

通过压力升高和下列方法之一, 提供EO气体已进行灭菌柜室的证据:

i) Mass of EO used (see D.10.2 i);EO使用的重量

ii) Direct measurement of the concentration of EO;EO浓度的直接测量

iii) Volume of EO used.EO使用的体积

3) sterilizer chamber temperature;灭菌柜的温度

4) exposure time;暴露时间

5) temperature of the sterilization load;灭菌产品的温度

6) an indication of the satisfactory operation of the chamber gas circulation system (if used) during exposure;暴露期间柜室内气体循环系统（若采用）正常运行的状态;

g) post exposure flushing (if used):暴露后清洗(如采用)

1) depth (ΔP or terminal pressure) and rate (ΔP/time) of attainment of vacuum;清洗压力的深度和真空速率

2) pressure (ΔP or terminal pressure) and rate (ΔP/time) of attainment of pressure associated with inert gas/air/steam;与惰性气体/空气/蒸汽相关的压力和速率。

3) number of times of repetition and any variations in successive repetitions;

重复的次数和重复时的任何变化。

h) aeration (if used):通风(如采用)

1) time and temperature within the chamber and/or room;柜室内或房间内的时间和温度;

2) pressure changes (if any) within the chamber and/or room;柜室内和/或房间内的压力变化

3) rate of change of air or other gas;空气或其他气体的更换频率;

4) temperature of the sterilization load.灭菌产品的温度

D.9.5.4 The validation report(s) should also include or reference the

following:

确认报告应包含或参考下列：

— The specifications for the sterilizer and the sterilization process;

灭菌柜和灭菌过程的技术指标

a) the IQ/OQ data;IQ/OQ数据；

b) the records, physical and microbiological, of all PQ runs;

整个PQ运行的物理和微生物记录；

c) an indication that all gauges, recorders, etc. were calibrated and within their specifications;

所有压力表、记录仪等已经校验且在有效期内。

d) provision for future review and requalification;

审核和重新验证的规定

e) the validation protocol(s)/procedure(s);确认方案/程序

f) the documented procedures used;使用的文件化的程序

g) documented operating procedures including process control limits;

包括过程控制极限的文件化的操作程序

h) if a failure occurred, a description of the issues, the corrective action taken, and the effect of the failure on the intent of the validation;

如果故障的产生，这个问题的描述，开展的纠正措施和对确认的影响。

i) if a deviation to the protocol occurred, details of this deviation and an assessment of its impact upon the validation and its results.

如果发生针对方案的偏差，偏差的详细信息及对确认及其结果的影响的评估。

9.5.5 If parametric release is to be used, the validation report shall also specify:

如果采用参数放行，确认报告应明确：

a) the value and tolerances for chamber humidity by direct measurement during conditioning;

处理期间的通过直接测量的柜室湿度值及其公差。

b) the value and tolerances for the EO concentration determined from direct analysis of chamber atmosphere using analytical methods to establish the process specification for routine processing.

用柜内空气分析系统直接测定的EO浓度值和公差来建立日常加工的过程规范。

The sampling shall be conducted at defined intervals sufficient to verify the required conditions throughout EO exposure.

应在规定的时间间隔内进行采样，以充分验证整个EO作用时间内的所需条件。

c) temperature of the chamber; recorded from two separate monitoring locations.

柜室温度；用柜室的二个分开的监视器记录；

D.9.5.5 Parametric release is a product release method wherein product is considered to be sterile if the essential physical processing parameters are in conformance with the specifications established during the validation for the specific product(s) in a defined load. Parametric release is based upon a documented review of processing records rather than the testing of biological indicators or PCDs.

如果，必要的特定的产品用规定的装载的过程参数与确认的一致，参数放行是认为产品为无菌的的一种产品放行的方法。参数放行的基础是在于过程记录的记录审核，而不是生物指示剂或PCD的试验。

The values and tolerances for both RH and EO concentration might need to be generated after review of a predefined number of routine cycles. During this evaluation period, BI’s might be used as part of the routine monitoring and control of loads processed. The rationale for the number of runs selected

should be justified and recorded. This can be influenced by uniformity of the load, existing data, seasonal variations or frequency of sterilization.

日常周期的预定的编号审核后，应产生湿度和EO浓度的值及其公差。在这个评估周期期间，BI可能用于日常监测和装载控制的一部分。应说明和记录选择的运行编号的合理理由。这可能受装载的均匀性、现有的数据、季节变化和灭菌频率的影响。

EO sterilizers used in health care facilities might not be adequately equipped to permit parametric release of product.

医疗保健机构使用的灭菌柜可能没有允许产品参数放行的装置。

9.5.6 A process specification including the process parameters and their tolerances shall be established for routine processing based upon the documentation generated during the validation. This process specification shall also include the criteria for designating EO processed product as conforming product and approved for release.

应建立一个包括过程参数及其公差的过程规范，使日常加工能满足确认期间产生的记录。该过程规范同时应包括指定的已用EO灭菌的产品的放行批准的准则。

10 Routine monitoring and control 日常监视和控制

10.1 The purpose of routine monitoring and control is to demonstrate that the validated and specified sterilization process has been delivered to the product.

日常监视和控制是为了证明，灭菌产品已经满足了确认和规定的灭菌过程

10.2 Data shall be recorded and retained for each sterilization cycle to demonstrate that the sterilization process specification has been met. These data shall include at least the following:

应记录和保存每个灭菌周期的数据，以证明已满足灭菌过程规范。至少应包含下列数据：

NOTE For practical purposes, rates can be determined as the time taken (with tolerances) to attain a specified pressure change.

a) the minimum temperature of product entering the sterilization process and/or the defined conditions used to acclimate the load;

进入灭菌过程的产品的最低温度，和/或规定的用于适当装载的条件；

a) The temperature of products entering the preconditioning area should be at or above the minimum temperature specified or the defined conditions of storage should be met. If the product has been exposed to extreme temperatures, for example during transport, it might be necessary to store the product prior to preconditioning, or extend preconditioning time to allow the internal temperature and humidity to be within acceptable ranges.

NOTE The minimum temperature of products entering preconditioning or the storage conditions are defined during PQ.

进入预处理区的产品温度应等于或高于规定的最低温度，或应满足规定的贮存条件。如果产品暴露于极端温度，如运输期间，在预处理前可能需要贮存产品，或延长预处理时间以允许内部的温度和湿度达到可接受范围内。

注，产品进入预处理区的最低温度或贮存条件在PQ时定义。

b) temperature and humidity within the preconditioning area (if used), monitored and recorded from a specified position;

预处理区内的温度和湿度，规定部位的监视和记录；

b) The reference position for routine monitoring of temperature and relative humidity during preconditioning should be correlated to the location at which it is most difficult to achieve the desired conditions. Monitoring data for the operation of the preconditioning area should be reviewed in conjunction with other data for the release of product.

预处理时的温度和相应的湿度日常监视参考位置应是所需的条件最难达到的位置。预处理运行的监视数据的审核应与其他产品放行数据相结合。

c) time of commencement of preconditioning and of removal of load from preconditioning (if used) of each sterilization load;

预处理开始的时间和每个灭菌产品从预处理转移的时间

d) elapsed time between removal of the sterilization load from preconditioning (if used) and the commencement of the sterilization cycle;灭菌产品从预处理到灭菌周期开始的间隔时间;

e) chamber humidity during conditioning and/or humidity dwell phases by pressure, pressure rise (ΔP) and/or direct monitoring;

处理期间的柜室湿度，和/或保湿阶段的压力上升和/或直接监视;

e) The humidity is typically calculated by measuring pressure changes. (See also AAMI TIR15.[24]) The humidity in the chamber is typically calculated by measuring the partial pressure of water vapour injected into the chamber. The relative humidity value is then determined using the steam tables by a ratio of the partial pressure to the saturated vapour pressure for the actual cycle process temperature. This will indicate the relative humidity value in the head space of the chamber and will be accurate until load or other reactions impact the actual water vapour content in the head space. Consideration should be given to the amount of moisture introduced into the chamber with the load from preconditioning.

湿度通常可以通过测量压力的变化来计算。(见AAMI TIR15.[24])。柜室内的湿度通常通过测量注入柜室的水蒸汽的局部压力来计算。然后利用蒸汽表，按实际循环过程温度的部分压力对饱和蒸汽压力的比例来确定相对湿度值。 这样计算出来的值为柜室顶部空间的相对湿度值，在负荷或其它反应影响顶部空间的实际水蒸汽含量前，这一值是精确的。应考虑装载从预处理带入的湿气的数值。

f) conditioning time;

处理时间

g) indication of the satisfactory operation of the chamber gas circulation system (if used) during EO injection and during exposure;

EO注射和暴露期间柜室内空气循环系统运行状态。

g) Forced gas circulation is particularly important when gas mixtures are used in order to ensure uniform conditions are maintained and to avoid stratification of gases that might have an impact on microbial lethality. (See D.6.3.2).

当使用混合气体时，为了保证保持均匀的环境以避免灭菌的气体对微生物杀死力的影响，迫使气体循环尤其重要。

h) temperature and pressure in the chamber throughout the sterilization cycle;

整个灭菌周期灭菌柜室内的温度和压力

i) If pressure is used as the primary control measure, the requirement for the secondary measure is only to confirm admission of EO to the chamber by at least one of the following:

如果压力作为主要的控制措施，那么，通过下列措施之一对EO进入柜室进行管理；

1) the mass of EO used (see D.10.2 i);EO重量

2) the direct measurement of the concentration of EO in the sterilizer chamber;灭菌柜室内直接测定的EO浓度

3) volume of EO used;EO体积

i) Pressure rise of EO injection (ΔP) provides an indirect measure of the mean EO gas concentration in the available space within the sterilizer chamber. As EO concentration is a key variable affecting the efficacy of the sterilization process, it is considered essential that a separate second system be provided for documenting that the pressure rise is due to EO admission (see AAMI TIR15[25] for more information). During EO injection and EO exposure phases of the sterilization process, EO is absorbed by product and packaging materials, which influences the correlation between the control measure (pressure differential) and the secondary measure (i.e. mass of EO dispensed or direct measure of EO concentration).

EO注入时的压力上升，提供了灭菌柜内可用空间的EO浓度的间接测量。当EO浓度是影

响灭菌过程效果的关键变量时，需考虑独立的第二系统，用以提供由于EO导入而引起压力上升的记录(更多的信息见AAMI TIR15[25])。灭菌过程的EO注入和暴露阶段，EO被产品或包装材料吸附，影响控制测量(压力差异)和辅助测量(如，导入的EO团块或EO浓度的直接测量)的关联性

j) EO-injection time EO注射时间

j) Since EO injection times can vary from cycle to cycle, it is common practice to specify a time range for an acceptable EO injection time.

由于各个周期之间EO注入时间可能是不同的，通常的做法是规定一个可接受的EO注入时间的范围。

k) inert gas injection, if used;惰性气体的注射

l) exposure time;暴露时间

m) time taken to evacuate the chamber;EO疏散柜室所需的时间

m) The time taken for evacuation immediately after EO exposure can vary from cycle to cycle; it is common practice to specify a range for acceptable evacuation time.

EO暴露后用于EO疏散柜室所需的时间可能每一次都变化，通常的做法是规定一个可接受的搬离时间的范围。

n) time and pressure changes during post exposure flushing;

暴露后清洗期间的时间和压力变化;

o) time, temperature, pressure changes (if any) during aeration.

通风期间的时间、温度、压力变化;

10.3 If biological indicators are used in routine monitoring, they shall comply with 8.6 and 8.7.

如果日常监视使用生物指示剂，应符合8.6和8.7的要求.

If the PCD that is used for routine release is different from that used in

the MPQ, it should be at least as resistant to the process as is the PCD used in the MPQ.

如果用于日常放行的PCD与用于MPQ的PCD不同，用于日常放行的PCD的过程抗力应不低于用于MPQ的PCD。

D.10.3 Observations of growth from biological indicators not attributable to failure to meet physical process specifications should be analysed; this can lead to a need for process or equipment modifications, and for the PQ to be repeated.

应分析未归因于满足物理过程规范的BI的生长观察。这能导致需要过程或设备的改进，和重新进行PQ。

10.4 If chemical indicators are used in routine monitoring, they shall comply with 8.8.

如果在日常监视中使用化学指示剂，应符合8.8的要求；

Chemical indicators shall not replace biological indicators for product release or be used to support a rationale to release a load parametrically.

化学指示剂应不能代替微生物指示剂用于产品的放行，或用于装载参数化的依据；

D.10.4 The following guidance is provided for health care facility applications:

为医疗保健机构的应用提供下列指南：

External chemical indicators in health care facilities: Sterilizer indicator tape, an indicating label or an indicating printed legend should be affixed to or printed on each package assembled by the health care facility. The purpose of external chemical indicators is to differentiate between processed and non-processed items. They do not establish whether the parameters for sterilization were achieved. Indicators should be of Class 1 specification in accordance with ISO 11140-1.

Internal chemical indicators in health care facilities:

a) An internal chemical indicator can be used within each package to be sterilized. If used, the chemical indicator should be placed in that area of the package considered to be the least accessible to EO, heat, and humidity penetration; this might or might not be the centre of the pack. While internal chemical indicators do not verify sterility, they allow detection of procedural errors and equipment malfunctions. The use of chemical indicators that respond to all the parameters of the EO process is beneficial.

b) The internal chemical indicator is retrieved at point-of-use and interpreted by the user. The user should be adequately trained and knowledgeable about the performance characteristics of the indicator in order to make an informed decision based on the result shown.

c) If the interpretation of the indicator suggests inadequate EO processing, the contents of the package should not be used. The complete unused package, including load identification and the chemical indicator, should be returned to the processing department for appropriate follow up. The results of the physical monitoring, chemical indicators elsewhere in the load, and the biological monitoring, should be reviewed, in order to reach a conclusion as to whether the entire load should be recalled or not. Records of this review should be retained. A single non-responsive or inconclusive indicator should not be considered as evidence that the entire load is non-sterile. Chemical indicators can indicate problems associated with incorrect packaging, incorrect loading of the sterilizer, overloading of the sterilizer chamber, malfunctions of the sterilizer, incomplete delivery of the sterilization parameters, or inadequate preconditioning. The “pass” result of a chemical indicator does not prove that the item where the indicator is placed is sterile.

d) Indicators should be of Class 3, 4, 5 or 6 in accordance with ISO 11140-1.

10.5 If parametric release is performed, the following additional data shall be recorded and retained:

如果执行参数放行，应记录和保存下列附加数据：

D.10.5 Parametric release is a method of releasing product from sterilization as sterile without the use of BIs, relying instead on a demonstration of conformity of the physical processing parameters to all

specifications. Therefore, data are gathered for additional processing parameters such as direct analysis of chamber relative humidity and EO concentration, in order to ensure that the sterilization process has met specification.

参数放行是一种在未使用BI情况下的产品按无菌放行的方法，仅依据物理过程参数对全部规范的符合性的证明。然而，为了确定灭菌过程已满足规范要求，作为附加过程参数如柜室直接测定的相对湿度和EO浓度数据的收集。

a) temperature in the chamber from a minimum of two locations throughout the sterilization cycle;整个灭菌周期内至少二个位置的柜室温度；

a) Temperature measurement.温度测量

The requirement to measure temperature within the sterilizer from a minimum of two locations is established in order to ensure that an undetected fault in a temperature sensor does not lead to the inadvertent release of an improperly processed load. If there is a difference in the two temperature data points, the acceptable temperature difference should be defined within the processing specification. If either the controlling or the monitoring sensor do not meet specification and an investigation cannot determine the accuracy of the chamber readings, the load is rejected

为了确保未被发现的温度传感器故障不会导致不适当过程装载的意外放行，应规定至少二个部位测量灭菌柜内温度的要求。如果，二个温度数据点有差异，在过程规范中应规定可接受的温度差异。如果控制或监视传感器中的一个不能满足规范的要求，并且调查不能证明柜室读数的准确性，这个装载应拒绝。

b) chamber humidity during conditioning as determined by direct measurement;

处理期间的直接测量的柜室湿度；

b) Humidity measurement.湿度测量

Direct analysis of the head space for relative humidity can be performed using electronic sensors, Gas Chromotography (GC), Infrared (IR) or other spectroscopic methods currently available to indicate water vapour concentration and calculation of the relative humidity value. The benefit of these methods is the real-time indication throughout the conditioning phase. Electronic sensors require periodic calibration to offset the effect of exposure to the EO gas and can require replacement after repeated exposures to EO due to irreversible deterioration of materials currently utilized as sensing elements.

可用电子传感器来完成相对湿度的顶部空间的直接测量，GC、IR或其他具有指示水蒸汽浓度和相对湿度值计算的光谱方法。这些方法的好处是贯穿处理阶段的即时显示；电子传感器应定期校验以排除暴露于EO气体的影响，和要求重复暴露于EO后由于作为传感元素使用的材料不可逆的老化而引起的更换。

c) the EO concentration, determined from direct analysis of chamber atmosphere using analytical methods at defined intervals sufficient to verify the required conditions throughout the exposure time.整个暴露时间内的在规定的时间间隔内用柜室空气分析系统直接测定的EO的浓度。

c) EO gas concentration measurement.EO气体浓度的测量

The frequency of analysis required to demonstrate that the minimum EO concentration is maintained throughout EO exposure should be established during the PQ studies. Monitoring throughout the EO exposure dwell period should also be done as part of the validation, in order to determine how the EO concentration changes over time. The results of this analysis are specific to the product and load configuration being analysed. The analysis performed during the PQ study will result in documented specifications for how often direct analysis should be performed during the cycle. It is recommended that when direct analysis of EO concentration is performed, at a minimum, direct analysis of EO concentration be performed during the first and last portions

of EO exposure.

在PQ研究期间，应规定在EO暴露过程中检测EO浓度的频次。为了测定EO浓度变化结束的时间，监视EO暴露时间也是确认的一部分。检测结果只针对特定的产品和装载方式。

Particular attention should be given to the measurement and documentation of humidity during conditioning and that of EO concentration during exposure. The EO sampling device providing direct EO concentration measurement using IR, GC, microwave, and other similar technologies should be positioned in a location to represent the EO gas concentration within the sterilizer chamber. However, it is important to understand that this measurement provides an EO concentration at that position in the chamber throughout the entire exposure phase without any restrictions of reactivity effects or load impact. The reproducibility and accuracy of the results from direct analysis should be determined during PQ. Routine cycle analysis should fall within the determined range for the cycle to be acceptable.

It can be necessary to introduce an equilibration time at the start of the EO dwell phase of the cycle to allow the chamber concentration to stabilize as the EO gas is distributed throughout the chamber and penetrates into the void spaces in the load.

NOTE 1 An electronic sensor measures EO gas concentration at only one sample site, whereas the calculated EO gas concentration represents the mean EO gas concentration within the space (volume) available for EO gas molecules to reside. Due to several factors, such as EO sensor dynamic performance characteristics, placement of the EO sensor within the volume occupied by the EO gas molecules, potential stratification within the chamber especially when the sterilant is made up of both EO and diluent gas molecules, selective absorption and adsorption of EO in the load and the volume taken up by the

load, the values obtained by calculating the mean EO gas concentration can differ considerably from the direct measured value.

NOTE 2 Health care facilities do not routinely use parametric release.

11 Product release from sterilization产品的灭菌放行

11.1 The criteria for designating conformance of the sterilization process used for a particular sterilization load shall be documented. The criteria shall include:

判定特定被灭菌物品灭菌过程合格的准则应形成文件。这些准则应包括：

a) confirmation that the data recorded during routine processing meet the sterilization process specification;

确定记录的常规处理数据符合灭菌过程规范要求；

b) confirmation of no growth of the test organism from any biological indicator (if used).

确定全部生物指示物的测试无微生物生长（若采用）。

NOTE Formal release of the load from sterilization could require results from other tests (e.g. EO residuals, endotoxin, physical testing, etc.) before product can enter the distribution chain.

产品进入销售渠道前，产品灭菌的放行可对其他试验的结果作出要求(如，EO残留量、内毒素，物理试验等)。

D.11.1 This confirmation should include a formal review of the process documentation by a designated individual (or by a validated automated process) to verify and document that the physical cycle variables are within the tolerances defined in the sterilization process specification. If parametric release has been approved and used, product can be released based on compliance

with specified process parameters.

这个确认包含指定人员(或由确认的自动化过程)由对过程记录的正式审核，以证明和记录物理周期变量是在灭菌过程规范中规定的公差内。如果已使用的批准参数放行，只要符合规定的过程参数就能放行产品。

Routine release of a product following sterilization can be based on a review of electronic records in lieu of paper records. Likewise, required signatures can be made electronically. Users of electronic signatures and records should be aware of, and should meet, national and/or international requirements for this type of documentation. The review of processing records and the decision to release should be performed by qualified individuals.

灭菌过程的常规放行可在电子记录代替纸质记录的审核的基础上进行。同样，要求的签名可以是电子的。电子签名和记录的使用者应了解并满足国家和/国际对文件类型的要求。过程记录的审核和放行的决定应由合格(有经验)的人员实施。

11.2 If a process does not fulfil all of the conformance criteria above, the cause shall be investigated. If repair or alteration to the equipment is required, the necessary qualification shall be performed before this process can be used again.

如果过程不能满足上述全部要求，应调查原因；如果设备经过了维修或调试，再次灭菌前应进行必要的验证

11.3 Product shall be considered as non-conforming and handled in accordance with the applicable clauses of ISO 13485 if one or more of the conformance criteria of 11.1 are not fulfilled. In the event of a positive BI, it is not acceptable to release product based on acceptable results of a product test for sterility.

如果不能满足11.1的一条或多条接收准则，产品应判定为不合格，并按ISO13485适当条款进行处置。如果有阳性的BI出现，产品的无菌试验不能作为产品放行的依据。

The non-conformity shall be addressed per documented procedures.

应按文件化的程序来处置不合格品

D.11.3 Failure to meet the physical specification or the observation of growth of indicator organism from BIs (if used) should lead to the sterilization load being quarantined and the cause of the failure being investigated. This investigation should be documented and the subsequent handling of product should be in accordance with documented procedures.

不符合物理规范或出现BI的微生物生长，应隔离灭菌产品并进行失败原因的调查。调查应记录，及随后的产品处理应符合文件化程序的要求。

If a controlling or monitoring sensor has failed, the run should be rejected, unless

如果控制或监视传感器故障，应拒绝这个运行，除非

a) there is an assignable cause for the failure, and

故障是可接受，和

b) data from the remaining sensors are within specification.

剩余的传感器内的数据是在规范要求内。

If the decision is to reprocess the load, the suitability of the product and its packaging system for resterilization should be established. The effect of repeated exposure to the sterilization process on product functionality and levels of residual EO, and/or reaction products, should be considered. Records of the original sterilization should be traceable from the re-sterilization records. (See 7.2.2).

如果决定对产品进行重新加工，应确认重新灭菌对产品及其包装系统的适应性。应考虑重复暴露于灭菌过程对产品功能和EO残留水平，和/或反应的影响。重新灭菌的记录可追溯到初始灭菌记录。

If the effect of repeated exposure on the packaging system is not known, product should be repackaged before resterilization.

如果不清楚重复灭菌对产品包装系统的影响，产品在灭菌前应重新包装。

11.4 If saleable product is used in validation studies the requirements for release of this product for distribution shall be generated before the start of the validation activities. It is important to assess the effect of repeated exposures to the validation/sterilization processes on product and packaging functionality, and levels of residual EO and/or reaction products prior to release.

如果用可以销售的产品来做确认，则应在确认开始前对产品的放行条件作出规定。产品放行前，确认/灭菌过程中的重新暴露对产品及包装功能，和EO残留量的水平和/或反应的影响的评估是十分重要的。

If saleable product is used in MPQ studies, then procedures shall be established to ensure the product is subjected to a full exposure sterilization process and formal review of its acceptance prior to release to market.

如果可销售产品用于MPQ的研究，那么，应建立程序以保证产品经过了整个暴露的灭菌过程(一个全周期)和在产品投放市场前的正式的可接收性审核。

NOTE See Annex E for information about single lot release.附录E给出了单一批放行的指南。

12 Maintaining process effectiveness保持过程有效性

12.1 General通则

12.1.1 The continued effectiveness of the system for ensuring the condition of the product presented for sterilization (see 7.3.1) shall be demonstrated.

应证明确保灭菌产品(见7.3.1)的系统的持续有效性。

D.12.1.1 To ensure that the sterilization process continues to deliver the required product SAL, it is necessary to evaluate any changes to the product and packaging, the processes and equipment. The use of a comprehensive product and process change control system is recommended.

为确认灭菌过程能持续达到规定的产品SAL，需要评估产品和包装、过程和设备的任

何变化。建议使用全面的产品和过程变化控制系统。

One parameter commonly monitored to ensure the continued ability to sterilize the load is the product bioburden. The bioburden should be monitored per ISO 11737-1. If significant changes are observed in the number and/or types of microorganisms, their possible effect on the ability of the sterilization process to adequately sterilize the load should be evaluated.

为保证持续的灭菌能力，产品生物负载通常是一个需监视的参数。应按ISO11737-1的要求监视生物负载。如果发现微生物的数量和种类有明显的变化，应评估这个变化对灭菌过程的影响。

In a health care facility, it is recommended that there be a periodic review of the data on the effectiveness of the cleaning/decontamination process, to confirm that the process is still effective and provides adequate bioburden reduction in preparation for the subsequent sterilization process.
Decontaminated medical devices should be visually examined for cleanliness prior to terminal sterilization. Medical devices that are not clean should not be sterilized. Policies and procedures should be in place to ensure that medical devices are adequately decontaminated prior to sterilization (see ISO 17664 and the ISO 15883 series).

It is essential for health care facilities to obtain from the manufacturers detailed reprocessing instructions specific to the medical device, e.g. disassembly. Policies and procedures should be in place to ensure that medical devices are decontaminated.

12.1.2 The accuracy and reliability of the instrumentation used to control and monitor the sterilization process shall be verified periodically in accordance with 4.3.3.

应按4.3.3的要求对用于控制和监视灭菌过程的仪表的准确性和重现性进行定期的校验；

D.12.1.2 A documented program for calibration of instrumentation used to control and monitor a sterilization process is necessary to ensure that the process continues to deliver product with the required SAL and performance characteristics.

需建立一个文件化的用于控制和监视灭菌过程的仪表的校验计划，以持续确保要求的灭菌产品SAL和性能特征。

12.2 Maintenance of equipment设备保养

12.2.1 Preventative maintenance shall be planned and performed in accordance with documented procedures. All procedures shall follow manufacturers' recommendations as well as any pertinent national, regional or local requirements.

应按文件化程序的要求对设备的保养建立计划并实施。全部程序应遵循制造商的建议以及适用的国家、地区或地方规章。

D.12.2.1 In order to be effective, preventive maintenance activities should follow a defined schedule based on the manufacturer's recommendations and the performance of the equipment. The procedures should be documented, and maintenance personnel should be trained.

为了保证有效的，应参照制造商的建议和设备特性建立保养计划，并按保养计划对设备进行预防性保养。保养程序应文件化，保养人员应经培训。

Equipment to be maintained and/or calibrated on a routine basis can include, but is not limited to, the following preconditioning, chamber and aeration equipment:

预处理、柜室和通风设备的日常保养和校验包括，但不限于:

a) gaskets and seals;垫圈和密封圈

b) monitoring gauges;监视的压力表

c) EO monitoring equipment (i.e. environmental and/or chamber);

EO监视设备(如，环境和/或柜室)

d) door safety interlocks;门的安全联锁装置

e) safety pressure relief valves or rupture discs;

压力释放安全阀或断裂盘

f) filters (for periodic replacement); 过滤器 (定期置换)

g) volatizers/vaporizers;蒸汽器/汽化器

h) chamber jacket re-circulation system; 柜室夹层再循环系统

i) chamber jacket system; 柜室夹层系统

j) audible and visual alarms; 声光报警

k) temperature and humidity sensor equipment;温度和湿度传感设备

l) boiler system for steam and heat supply; 蒸汽加热系统和供热系统

m) evacuation equipment (vacuum pumps);抽真空设备(真空泵)

n) weighing scales; 称重设备

o) valves; 阀

p) pressure transducers; 压力传感器

q) timers;定时器

r) recorders;记录仪

s) air/gas circulation systems.空气/气体循环系统

12.2.2 Equipment shall only be used to process product after all specified maintenance tasks have been satisfactorily completed and recorded.

只有有效地完成全部规定的保养项目并记录后，设备才能加工产品。

D.12.2.2 Sterilization equipment that is not calibrated or is not properly

maintained can generate an inaccurate record of the process parameters during the sterilization cycle. If these data are used for product release, it could result in loads being released that have not been adequately sterilized.

未校验或未按要求保养的灭菌设备在灭菌周期期间能产生一个不准确的过程参数记录。如果这些数据用于产品放行，可能导致放行的产品未彻底灭菌。

12.2.3 Records of maintenance shall be retained (see 4.1.2).

保养的记录应被保存。

12.2.4 The maintenance scheme, maintenance procedures and maintenance records shall be reviewed at specified intervals by a designated person and the results of the review shall be documented.

保养方案、保养程序和保养记录应由指定人员进行定期审核，并记录审核的结果。

D.12.2.4 It is necessary to periodically review the maintenance records and to make any adjustments that are indicated by the data.

需定期审核保养记录，并根据显示的数据进行调整。

12.3 Requalification 重新验证

12.3.1 IQ, OQ, PQ and subsequent requalification(s) shall be reviewed annually to determine the extent of requalification that is necessary. This shall include an assessment of the need to reconfirm the product SAL through microbiological studies. The outcome of this review, including the rationale for decisions reached, shall be documented.

应每年评审IQ,OQ，PQ和并确定随后的重新验证，以确定必需验证的范围。应包括重新通过微生物研究确定产品SAL的需求的评估。应记录评审的结果，包括所作决定的理由。

D.12.3.1 Review of IQ should include confirmation of the acceptable calibration status of control and monitoring equipment. The change control and preventive maintenance programs indicate that no modifications of, or significant changes to, the sterilizing equipment have been made that could

affect the process.

IQ评审应包括监视和控制设备的可接受状态的确定。变动的控制和预防性保养计划表明灭菌设备未发生影响灭菌过程的设备调整，或明显的变化。

12.3.2 Requalification of a sterilization process carried out with specified equipment shall be performed at defined intervals against specified acceptance criteria and in accordance with documented procedures. These intervals shall be justified.

应按照规定的接收准则和形成文件的程序，在规定的时间间隔对规定设备进行灭菌过程重新确认。该时间间隔应予以说明。

D.12.3.2 Review of OQ should include an assessment of the equipment performance and engineering changes that were made during the year to ensure that the results from the original OQ are still valid (see Figure D.1).

OQ的评审应包括一年来发生的设备性能和工程变化，以确保原先的OQ的结果仍是有效的(见 FigureD.1)

In order to do so, it is common practice to perform periodic requalification of equipment and should include:

为了证明原先OQ的有效性，通常的做法是定期再验证设备，并应包括:

a) review of IQ status of equipment;设备的IQ状态的评审;

b) assessment of trends in equipment performance;设备性能趋势的评估

c) temperature and relative humidity profiles of the preconditioning areas (if used);预处理区的温度和相对湿度分布。

d) chamber temperature profile;柜室温度的分布

e) temperature profile of the aeration areas (if used).

通风区温度分布;

These requalification exercises should indicate no significant changes in the performance of preconditioning (if used), chamber or aeration areas since the

previous (re)qualification. If equipment changes are necessary as a result of these exercises, requalification of OQ might need to be repeated.

重新验证报告应说明预处理柜室或通风区自上次验证以来无明显的变化。如果报告认为设备已发生变化，必须重新进行OQ验证。

NOTE For large preconditioning or aeration rooms containing multiple sterilization loads, the extent of requalification can be reduced if there have been no significant changes in equipment. The rationale for reduced requalification is documented.

注,对于较大的包含多种灭菌产品的预处理室或通风室来说,如果设备无明显的变化,可以减少重新验证的范围。应记录减少重新验证的理由。

12.3.3 If requalification indicates that the sterilization process might no longer be capable of achieving the required product SAL, the cause shall be investigated and corrective and/or preventive action shall be taken. As part of the investigation, the effect on the achievement of the specified SAL for previously processed loads of product shall be considered and a risk assessment undertaken on their suitability for use. If the investigation shows that the required SAL can no longer be achieved then a new MPQ/PPQ shall be performed to re-establish the required SAL. The investigation and subsequent actions shall be recorded.

如果重新验证表明，灭菌过程可能不能达到要求产品SAL，应调查原因，并开展纠正措施和/或预防措施。当调查发现未全部达到时，应考虑按设定的灭菌过程达到规定的Sal的能力，并对灭菌过程进行风险评估。如果调查表明不能达到规定的SAL时，应重新进行MPQ和PPQ以重新确认规定的SAL。调查及随后的活动应记录。

D.12.3.3 Review of PQ should include assessment that the sterilization process remains valid for the designated product(s).

PQ的审核应包括评价针对特定产品的灭菌过程的持续有效性。

Factors to be considered include, but are not limited to, the following:

需考虑的因素包括，但不限于下列：

a) review of IQ status of the equipment;设备的IQ状态评审；

b) review of OQ status of the equipment; 设备的OQ状态评审

c) confirmation that there have been no significant changes to the product design, manufacturing and packaging materials, PCDs, suppliers, manufacturing area or facility, load configuration, or manufacturing process that could affect product sterility;

证明可能影响无菌状态的产品设计、制造和包装材料、PCD、供应商、生产区域或工厂、装载方式或制造工艺未发生明显的变化。

d) confirmation that there has not been a significant increase in the product bioburden, and/or a change in the resistance of the product bioburden to the sterilization process, which might adversely affect the ability of the sterilization process to sterilize product to the specified SAL;

证明产品的生物负载，和/或产品生物负载灭菌抗力的变化及这些变化可能已影响了使灭菌产品达到规定SAL的能力没有明显的增加。

e) confirmation that individual sterilization processes have operated within specification since the last qualification;

证明自最后验证以来，灭菌过程在规范要求内运行。

f) confirmation that there have been no changes to the sterilization process that could affect product sterility;

证明可能影响产品无菌状态的灭菌过程未发生变化。

g) review of sterility failures of BIs or PCDs that have occurred where process specifications were met to determine whether requalification is warranted.

满足过程规范过程的BI或PCD的无菌失败的审核，以确定是否有必要进行重新验证。

Based on this review, the sterilization specialist should determine the extent of physical and microbiological requalification required. The review and

decision should be documented.

基于这个审核，灭菌专家应确定要求的物理和微生物重新验证的范围。审核和决定应记录。

There are three requalification options available as a result of the review:

作为审核结果，有三个重新验证的方案:

— *Full Qualification* – consisting of PPQ and MPQ.

全验证——包括PPQ和MPQ

This can be required in certain situations, e.g. following a significant change to product/packaging design or configuration (creating a new “worstcase” condition), process design or equipment/service.

在某些状况下要进行全验证，如，产品/包装设计或方式(产生一个新的‘最坏状态’条件、过程设计或设备/服务的明显变化。

— *No physical or microbiological qualification required* – In circumstances where no changes have been made to product, packaging, equipment/services and process, acceptable chamber performance and

engineering review, and the routine sterilization process has operated reliably in the intervening period, then professional judgment can be used to justify that no physical or microbiological requalification efforts need be performed before the next review.

无需物理或微生物验证——在产品、包装、设备/服务和工艺无变动，柜室性能和工程技术审核合格，常规灭菌工艺在介入阶段运行可靠的情况下，可用专业的判断的方法来证明在下一次审核前无需进行物理或微生物再验证。

— *Reduced MPQ/PPQ* – This can be necessary in certain situations, e.g. to verify continued appropriateness of the resistance of the internal PCD in the product load to the resistance of the product bioburden, or, after a defined interval, to provide evidence that there has been no inadvertent change since the previous requalification study. This would typically include, minimally,

one fractional or half cycle exposure including load temperature and humidity measurements. Fractional cycles in a developmental chamber can also be used to support a requalification program, but requalification of the production chamber should be performed in the production chamber.

减少的MPQ/PPQ - 在某些特定的情况下需进行减少MPQ/PPQ，如验证产品生物负载抗力与产品装载内的内部PCD抗力的持续相适应性， 或在规定的间隔后，需提供自上一次鉴定(再鉴定) 以来没有不利变化的证据。减少MPQ/PPQ最低限度一般为一个包括被灭菌物品温度和湿度测量的短周期或半周期。在试验性柜室的短周期也可用于支持再验证项目，但生产性柜室的再验证应在生产性柜室中进行。

It is recommended that a MPQ cycle and load temperature and humidity measurements (MPQ/PPQ) be performed at least every two years to verify that the documented paperwork review has captured any changes in the product or sterilization process.

建议至少每二年要进行一次MPQ的和装载温度和湿度的测量（MPQ/PPQ），以验证在文件化的评审已收集了产品或灭菌工艺的任何变化。

Requalification can also include verification that if the sterilization process specification is changed, then requalification of the sterilization process should include confirmation that product meets allowable limits for EO residuals as specified in ISO 10993-7.

如果灭菌过程规范发生改变，那么，灭菌过程的重新验证应包括产品满足ISO10993-7规定的EO残留极限的确认。

In all of the above cases, it is important to document the decisions taken as well as the rationale for those decisions, and to define the plan for future review of requalification.

在上述所有情况中，重要的是要记录所做的决定及决定的合理性，并制定将来的再验证评审的计划。

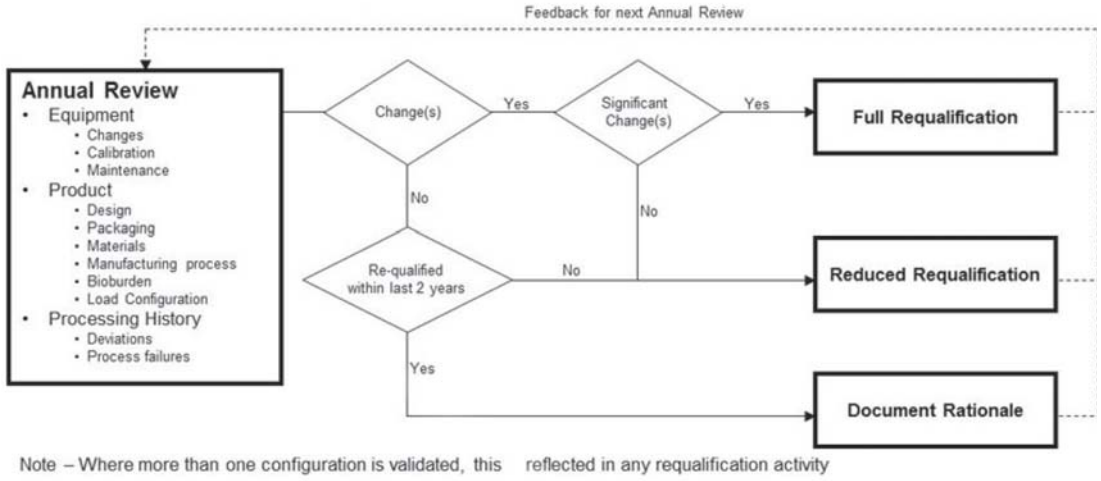

Figure D.1 — Requalification decision tree

12.3.4 Records of reviews of requalification data, reports and resulting corrective actions (if required) shall be retained (see 4.1.2).

重新验证数据评审的记录，报告和纠正措施结果应保存。

D.12.3.4 Requalification is performed to confirm that the cumulative effect of minor changes has not compromised the effectiveness of the sterilization process.

进行重新验证是确认轻微变化的累积影响未对灭菌过程的有效性造成损害。

Requalification can include verification that allowable product EO residuals as delineated in ISO 10993-7 are being met.

重新验证包括产品满足ISO10993-7规定的EO残留极限的验证。

It is important to formally assess the need for requalification of the sterilization process at least annually to ensure that inadvertent process changes have not occurred and to demonstrate that the original validation remains valid.

至少每年一次的灭菌过程的是否需要重新验证的评价是十分重要的，以确保未产生非故意的变化，以及证明原先的确认仍有效。

The requalification program should define acceptable ranges and levels of

variability in performance that are necessary to maintain the validity of the original validation from year to year.

重新验证计划应规定一年接着一年的保持原先确认有效性的性能变化的可接受的范围和水平。

D.12.3.5 An investigation should be initiated to try to determine the root cause(s) of a non-conformity.

应展开调查，以努力确定不合格的原因。

The impact of the non-conformity on the validity of the requalification should be assessed and the rationale for the decision(s) reached should be documented. Further activities pertaining to the requalification should proceed with proper quality system oversight.

应评估不合格对重新验证有效性的影响，以及记录所作决定的理由。进一步的有关重新验证的活动应按质量管理体系进行。

12.4 Assessment of change变化的评估

12.4.1 Changes to manufacturing operations, product, sterilization equipment and/or the sterilization process shall be assessed for their effect on the effectiveness of the sterilization process.

应评估生产作业、产品、灭菌设备和/或灭菌过程的变化对灭菌过程有效性的影响。

D.12.4.1 Events that might require requalification include, but are not limited to:

可能需要重新验证的变化包括，但不限于：

a) major sterilizer repairs and changes (replacing controls, major rebuilding or installation of major new components);

灭菌柜的大修和变化（重新放置控制器，关键部件的重建或安装）

b) changes to construction or relocation;构造的变化或搬迁；

c) unexplained sterility failures in routine sterilization;

日常灭菌时原因不明的无菌失败。

d) changes to product;产品的变化

e) changes to packaging;包装的变化

f) modification to the sterilizing agent and/or its presentation;

灭菌剂和/或其性能的更改

g) changes to presentation of product for sterilization or load configuration;
产品灭菌过程或装载方式的变化。

h) changes to load density.装载密度的变化

It is important to ensure that the reference load used in any requalification takes into account changes that might have been made to ensure that the reference load is representative of the revised product/configuration.

确保用于任何重新验证基准装载的变化已经考虑到以确保基准装载对改变的产品/装载具有代表性是重要的。

12.4.2 The appropriateness of the internal and/or external PCD in relation to the bioburden of the product shall be reconfirmed as a result of change (see 8.6 and 10.3) as appropriate.

当产品的生物负载发生变化时，应重新证明内部和/或外部PCD的合适性；

D.12.4.2 A requalification study could be necessary if a change has been made in materials, manufacturing location or processing method that can impact the product bioburden population or resistance. The study should demonstrate that product bioburden population or resistance has not increased to a level which might potentially invalidate the suitability of the internal PCD, or compromise achievement of the required product SAL.

如果那些能影响产品生物负载数量和抗力的材料、制造区域或工艺方法发生变化，需要进行重新验证。应证明产品生物负载数量和抗力的增加未导致内部PCD的不适用，或影响产品SAL；

12.4.3 The load and load configuration shall be re-evaluated following a change for its appropriateness, and the results of this re-evaluation shall be documented in accordance with 4.1.2.

应对变化后的装载和装载方式的适当性进行评价，应按4.1.2的要求记录重新评价的结果。

D.12.4.3 Where re-evaluation of the load and load configuration identifies changes that might impact on the efficacy of the sterilization process, then these changes should be incorporated into the requalification studies.

如果装载或装载方式的评价表明具有可能影响灭菌过程有效性的变化，那么，重新验证时应考虑这些变化。

12.4.4 The qualified sterilization process shall be reviewed whenever there has been a change to the sterilization process, the sterilization equipment or product that could alter the efficacy of the process (see 8.2).

每当可改变过程有效性(见8.2)的灭菌过程、灭菌设备或产品发生变化，应评审合格灭菌过程。

12.4.5 The magnitude of the change shall be considered in determining the extent to which process definition, IQ, OQ or PQ is undertaken.

确定过程定义、IQ、OQ或PQ的实施范围时，应考虑变更的程度。

12.4.6 The outcome of the assessment, including the rationale for decisions reached, shall be documented.

应记录评估的结果，包括所作决定的理由

12.5 Assessment of equivalence等效评价

12.5.1 Process Equivalence过程等效

Sterilization equipment that delivers the same process parameters, having undergone IQ and OQ, shall be qualified either.

已经实施了IQ和OQ,执行同样过程参数的灭菌设备也认为是合格的。

a) in the same manner as the original chamber, or

与原始柜室同样的方式；或

b) using a reduced MPQ that demonstrates the delivery of the required level of microbiological lethality and PPQ to demonstrate temperature and humidity uniformity of the load and control by the production chamber. The rationale for this reduced qualification shall be recorded and documented.

用减少的证明能提供规定的微生物杀死力水平的MPQ，以及用减少了的PPQ来证明装载温度和湿度的均匀性，并由生产性柜室来控制。应记录和文件化减少验证的理由。

The influence of different geographical locations on the product or load properties shall be determined.

应测定产品或装载形式中不同部位的影响。

D.12.5.1 Process equivalence is a method used to demonstrate that the same validated sterilization process is delivered by two or more pieces or sets of equipment. It does not require that the equipment be physically identical. Even if the parameters delivered by the equipment are not statistically identical, the processes delivered can still be equivalent if they are all capable of running the process within the defined, validated process limits (see AAMI TIR 28[26]).

过程等效性是一种用于证明同样的已验证的灭菌过程适用于二台或多台设备的方法。过程等效性不要求设备完全相同。即使设备的参数在统计学意义上不尽相同，但如果过程运行的能力在定义的、已验证过程的极限内，这个过程仍是等效的。

Process equivalence among multiple pieces of equipment is intended to minimize the amount of testing required to qualify the process. The sterilization process should be validated in one chamber. The remaining equipment can undergo reduced PQ if the remaining equipment has undergone installation qualification (IQ) and operational qualification (OQ) (see 9.2 and 9.3). Equivalence can also be used to reduce requalification of several pieces of equipment. The equipment used to deliver a sterilization process commonly consists of a

chamber or room and ancillary control systems. Sterilization process equipment might be located within a given processing facility or among several facilities. This equipment can be used independently to deliver the same process conditions and could be exactly the same design or might differ in size or in the extent of ancillary equipment.

多台设备的过程等效是为了尽量减少试验的数量。灭菌过程应在同一台柜室中进行。如果剩余的设备已经实施了IQ和OQ，可以接受减少了的PQ。等效也可用于减少少量设备的重新验证。用于提供灭菌过程的设备通常由柜室或房间及其辅助控制系统组成，灭菌过程设备可以安装在提供过程的工厂或几个工厂中的其中之一。这台设备能独立提供同样的过程条件，并可能是同样的设计或可能在外形或辅助设备的范围不同。

Process equivalence can be established through analysis of process data in combination with a microbiological evaluation. The process data should demonstrate that the candidate equipment is performing within an acceptable range of control (i.e. validated process parameters can be reliably delivered to the product). The data analysis should confirm that the process operates within the defined tolerances for the validated parameters. The microbiological evaluation will demonstrate that the

required SAL is achieved.

可以通过结合微生物评价的过程数据分析来建立过程等效。过程数据应证明候选设备在可接受的控制范围内运行(如，已验证的过程参数能可靠地提供于产品)。数据分析应确定过程在已验证参数的规定的公差内操作。微生物学评估将证明达到了要求的SAL。

12.5.2 Product

A product may be added to a validated process if deemed equivalent to or a lesser challenge than an existing qualified product or internal PCD. A technical review shall be performed comparing the candidate product with the product or PCD that was used to validate the existing EO process. The outcome of the technical review, including the rationale for decisions reached, shall

be documented. The requirements of 7.2 still need to be addressed for the product.

如果认为与目前的产品或内部PCD相同或较少的变动，产品是可以加的。待加产品与已验证过程的产品之间应作一个技术审核，应记录技术审核的结果，包括符合的理由。产品仍需要满足7.2的要求.

D.12.5.2 Criteria for process equivalence过程等效准则

Process equivalence can be established regardless of whether the equipment is located in the same facility or in different facilities. The criteria to be met prior to the establishment of a process equivalence program are:

无论设备安装在同一地方或不同地方都能建立过程等效性。过程等效性项目建立前应满足的准则是:

a) full validation of the sterilization process in at least one existing system according to the requirements of Clause 9;

根据章节9.的要求在至少一个现有系统中的灭菌过程的完整确认。

b) performance of the IQ and OQ studies demonstrating and documenting that all equipment has been installed in accordance with engineering specification requirements and operates in accordance with those requirements;

证明和记录全部设备已按技术规范要求完成了安装，并按这些要求运行的IQ和OQ研究。

c) definition of the process to include the tolerances allowed and documentation of all phases of the process; and

包括允许公差的过程定义，及过程全部阶段的文件；和

d) process data analysis associated with the validated tolerances for the candidate equipment and the original equipment.

候选设备和原设备之间的有关联的已验证的公差的过程数据分析;

D.12.5.3 Determination of process equivalence过程等效性测定

The equivalence of the sterilization process delivered by one piece of equipment to that delivered by another piece of equipment can be established by comparing the data obtained when running the same validated process in each piece of equipment. This comparison should include an evaluation of the equipment's capability to reproducibly deliver the desired process parameters when running a normal production load. Data obtained during the PQ on the process can also be used. The delivered parameters and tolerances should be those that were previously validated in the PQ of the sterilization process in the original equipment. The evaluation of equivalence involves performing a process analysis and evaluation as well as a microbiological evaluation.

通过比较在各自的设备中运行同样的验证过程中获得的数据，建立一台设备与另一台设备的灭菌过程的等效性。这个比较应包括，当运行正常生产装载时，设备重复提供预期过程参数能力的评估。等效性评估涉及执行过程分析和评估，以及微生物评估。

D.12.5.4 Process analysis and evaluation 过程分析和评估

An analysis of process data associated with a validated process in the candidate equipment and the original equipment is performed. Process data should be collected from the candidate equipment.

进行候选设备和原设备间关联的验证过程的过程数据分析。过程数据应从候选设备中收集。

These data should be compared with the parameter limits for that specific sterilization process and the results obtained in the PQ of the original equipment. The parameter limits are those established in the initial validation for the sterilization process (including all process requirements identified in this International Standard) in the existing equipment. The specifications, acceptance criteria, and pallet or load configuration should be the same as those defined for the initial PQ. The actual parameters to be evaluated in the equivalence determination are generally a subset of the entire process specification.

这些数据应与定义的灭菌过程的参数极限和在原设备的PQ中获得的结果比较。

参数极限是那些在现有设备中的灭菌过程(包括本标准中定义的全部过程要求)的初始确认的数据。规范、接收准则，和托盘或装载方式应与初始PQ定义的一致。

The parameters selected and the rationale for their selection should be documented. Statistical methods that evaluate both the central tendencies of the test data and the degree of variability of the data can be used in this evaluation. Examples of statistical analysis approaches are presented in AAMI TIR15. [24] The examples are illustrative only, and are intended to provide guidance on statistical calculations, normality requirements, and steps to take if the data fail a normality test. If the process analysis and evaluation do not meet the established acceptance criteria, then it is not possible to demonstrate process equivalence.

应记录参数的选择和选择的理由。评估试验数据的中心趋势和数据的变化程度的统计方法能用于评估。AAMI TIR15.提供了统计分析方法的例子。如果正常的试验数据失败，这些例子只是举例说明，是替代提供统计计算的指南的，正常的要求，和进行的步骤。如果，过程分析和评估不能满足建立的接收准则，那么，证明过程等效性是不可能性的。

D.12.5.5 Evaluation of preconditioning or aeration areas预处理或通风区的评估

The criteria for establishing process equivalence are the same for preconditioning or aeration areas, with the exception that humidity usually does not apply to aeration. An evaluation that compares the load temperature and humidity profiles within each environment should be performed. At a minimum, temperature and humidity uniformity within the load and the relationship of this uniformity with the corresponding set points and recorded control variables for the areas should be evaluated.

对预处理区或通风区来说,除了通风区通常不提供湿气,过程等效性的准则是相同的。应进行在每个环境内装载温度和湿度状况的比较的评估。最低限度，应评估装载内的

温度和湿度的均匀性，以及区域的均匀性与相应设置点和记录的控制变量的关系。

If the pieces of equipment use different set points or have different control limits, it might not be possible to declare that they are equivalent. Process equivalence for the preconditioning or aeration processes can be established if analysis of performance data concludes that conditions within the load meet the parameter limits (e.g. temperature distribution, residual levels, etc.) at the end of preconditioning or the end of aeration. Product EO sterilization residuals levels should be verified in the candidate aeration room/chamber/cell.

如果设备使用不同的设定点或有不同的控制极限，不能声称具有等效性。如果，性能数据的分析得出预处理或通风结束时装载内的条件满足参数极限(如温度描述、残留水平等)的要求的结论，预处理或通风过程的过程等效成立。

D.12.5.6 Evaluation of sterilization chamber performance灭菌柜性能评估

An evaluation that compares the delivery of process parameters for the load in the candidate equipment to the data obtained in the PQ or in production runs should be performed. The critical process and load parameters to be compared should be defined for the sterilization process before the evaluation is performed. These parameters are unique for each sterilization process but can include the following:

应实施一次候选设备的装载参数的提供与PQ或生产运行中获得的数据比较的评估。在评估实施前，应定义灭菌过程要比较的关键过程和装载参数。这些参数是每个灭菌过程特有的，但可以包括下列:

a) Load parameters:装载参数

1) product temperatures — temperatures achieved and their distribution within the load during EO dwell;

产品温度——EO驻留时装载内的温度及其分布。

2) product humidity — humidity achieved and its distribution within the

load at the end of conditioning.

产品湿度——处理结束时装载内的湿度及其分布。

b) Process parameters:过程参数

1) chamber humidity at selected times during the cycle (e.g. beginning and/or end of conditioning). This parameter can be measured directly or can be based on pressure rise due to steam injection;

循环时选定时间点(如处理的开始和/或结束)的灭菌柜湿度。湿度可以是直接测量或基于蒸汽的注入而压力上升。

2) chamber process temperature at selected times during the cycle (e.g. end of conditioning or during the EO dwell period);

循环时在选定时间点(如，处理结束或EO驻留期间)的灭菌柜的过程温度。

3) chamber EO gas concentration at selected times during EO dwell period during the cycle (if measured), or EO pressure rise or gas weight.

循环时EO保持期间在选定时间点的灭菌柜内的EO气体的浓度（如测量），或压力上升或气体重量。

c) Other process parameters that might be considered include:

应考虑的其他过程参数包括:

1) vacuum depth and rate of evacuation (ΔP/time) at selected times during the cycle;

循环时在选定时间的真空度和抽真空速率。

2) humidification time and steam injection rate (ΔP/time);

加湿的次数和蒸汽注入速率。

3) EO injection temperature and rate (ΔP/time) and the amount of EO used (weight, concentration, or pressure); and

EO注入温度和速率，以及EO使用量(重量，浓度，或压力)；和

4) air or nitrogen injection rate (ΔP/time).

空气或氮气注入速率。

An analysis of the process data are used to indicate that the processes are or are not equivalent in their ability to meet the existing process parameter limits and any additional acceptance criteria. The data generated should be analysed and compiled in a format that will allow for its use in future process equivalence determinations.

过程参数的分析是用于表明过程在满足现有过程参数极限和任何附加的接收准则的能力方面的是否是等效的。应分析，并用允许用于将来的过程等效证明的格式编辑这些产生的数据。

D.12.5.7 Microbiological evaluation 微生物评估

In the microbiological evaluation, a fractional or half cycle is performed to demonstrate that the sterilization process is capable of delivering the defined minimum specified product SAL in all the evaluated pieces or sets of equipment.

用一个短周期或半周期进行微生物学评估，以证明灭菌过程是有能力在整个灭菌柜中提供已定义的最小的确规定的产品SAL。

NOTE If the run used during process analysis was a fractional or half cycle and included microbiological monitoring, then the data can also be used for this evaluation.

注，如果过程分析使用的运行是一个包括了微生物监视的短周期或半周期，那么，这些数据也可用于微生物评估。

In addition to the delivery of the specified product SAL, additional factors that should be evaluated include any changes to the sterilization location or manufacturing location that might have an impact on the bioburden level of the product as presented for sterilization. Increased distances between the manufacturing facility and sterilization site might result in higher

bioburden levels, especially if the product will support microbial growth. Differences in manufacturing environments might lead to the manufacture of product with higher or more resistant bioburden levels than previously qualified, even if the product does not support microbiological growth. Another issue to be evaluated when shipping product between sites is the difference in shipping conditions, such as time in transit and seasonal effects (e.g. temperature, humidity, etc.). Holding of product under defined conditions to simulate shipping/transport conditions should be performed if required.

除了规定的产品SAL的提供，应评估其他因素，包括可能影响用于灭菌过程的产品的生物负载的灭菌场地和生产场地的变化的。生产工厂和灭菌场所的距离的增加可能导致生物负载水平，尤其在产品有助于微生物的生长的情况下。生产环境的不同可能导致比日常合格的产品具有更高或更具抗力的生物负载水平，即使产品不利于微生物生长。当销售产品的灭菌过程与销售条件不同时，如过境时间和季节影响(如，温度、湿度等)，应对不同条件进行评估。如是有要求，产品应保持在规定的模拟过境/销售条件下。

D.12.5.8 Results evaluation 结果评估

The results of the evaluation will determine whether the different pieces or sets of equipment perform equivalently. If the different pieces or sets of equipment are equivalent, then the requirement for a reduced MPQ has been satisfied through the testing that was already performed and no further qualification would be necessary. If the conclusion of either the process analysis and evaluation or the microbiological evaluation is that the processes are not equivalent, then the process should be declared “not equivalent” and a full PQ should be performed.

评估的结果将确定不同的设备是否可以等同地执行。如果不同的设备是等效的，那么，通过已经执行的试验，减少的MPQ的要求已经被满足，且不需要进一步的验证；如果，过程分析和评估或微生物评估的结论是不等效的，那么，应声明过程是‘不等效’的，应实施整个PQ。

D.12.5.9 Maintenance of equivalence 等效性保持

Maintenance of equivalence should include a review of changes to each piece of equipment, the manufacturing process, the product load, and the sterilization process to ensure that these changes do not compromise the overall determination of equivalence. This review should be conducted before changes are made and should be part of the change control process. If any process fails the periodic equivalence review, then it should be removed from the equivalence list and requalified on its own.

等效性保持应包括每个灭菌设备、生产过程、产品装载、和灭菌过程的变化的审核，以确保这些变化未削弱等效性的声明。审核应在变化产生前进行，应是变化控制过程的部分。如果任何过程不能满足定期的等效审核，那么，应从等效清单中去除，并且应重新验证。

D.12.5.10 Documentation记录

All decisions related to the outcome of the analysis determining whether candidate equipment can be declared equivalent to the existing sterilization process equipment should be documented. At a minimum, this documentation package should include:

声称候选设备是否与现有灭菌过程设备等效的全部与分析测定结果相关的结论应记录；至少，这些文件应包括：

a) The complete specification for the candidate equipment, which fully describes the equipment, operating specifications, and tolerances, and which refers to or provides a list of applicable operating procedures, calibration procedures, and maintenance schedules. This specification should include or reference the current IQ per this International Standard.

候选设备的完整的规范，规范包含设备的完整的描述、操作规范、及其公差，以及指明出处的适用的操作程序、校验程序员和保养计划的清单。规范应包括或参考按本标准建立的现有的IQ。

b) Evidence or assessment of the ability of the equipment to deliver the

intended process. The evidence or assessment should include or reference the current OQ.

设备提供替代过程的能力的证据或评介。证据或评价应包括或参考现有的OQ.

c) The result of the comparison between the candidate process equipment and the existing validated process equipment. This comparison should clearly demonstrate that all major systems and critical parameters were assessed, including statistical analysis (if used).

候选过程设备与目前已验证过程设备比较的结果。比较应清楚地声明，全部主要系统和评价过的关键参数，包括统计分析(若采用)。

d) Evidence or assessment of the product conditions during processing within the candidate equipment to demonstrate equivalence to the existing process.

在候选设备内加工期间的产品条件的证据或评价，以证明与目前过程的等效性。

e) Results of the evaluation of any additional factors that could affect the lethality of the sterilization process, as appropriate.

如适用，可能影响灭菌杀死力的任何附加因素评估的结果。

f) The documented conclusion that the candidate equipment is equivalent to the equipment specifically referenced in the current validation study to achieve the specified product SAL. This conclusion should include or reference any additional tests performed to supplement the existing validation study and any further testing performed for confirmation or qualification for routine release of product from the existing validated cycle (e.g. residual testing, functional testing on first three lots, etc.).

候选设备与已确认的能达到规定的产品Sal的设备是等效的文件化的结论。结论应包括或参考任何附加的目前确认的补充试验和确认或验证从目前已验证循环的产品日常放行的进一步试验(如，残留量试验，前三批的功能试验,等)。

g) Approval by the sterilization specialist and other individuals as required by the normal change control or process documentation control practices within

the organization.

由灭菌专家，或由组织内正常的变化控制或过程文件控制惯例要求的人员批准。

h) A list of applicable sterilizer operating procedures and specifications issued or changed to authorize use of the candidate equipment for routine processing of product.

适用的灭菌柜操作程序，和批准候选设备使用于日常产品生产的发放的或变更的规范的清单

D.12.5.11 Product 产品

D.12.5.11.1 Product family 产品族

A product family is a collection of products determined to be similar or equivalent for validation purposes. Although product families can be used for other reasons (EO residuals, bioburden, or biocompatibility) for EO sterilization, a product family usually refers to products that have been grouped together for the purposes of determining that the required SAL has been delivered to the products during the MPQ.

就确认目的而言，产品族是一个被证明是相似的或等效的产品的集合。尽管为了EO灭菌的其他理由(EO残留、生物负载，或生物学评价)而使用产品族，产品族通常参考，在MPQ时按产品的SAL分组在一起的产品。

An EO product family can consist of various combinations of similar products. For example, a product family might contain a series of catheters that differ only in their sizes or a variety of products that are made in the same environment with the same material. When products are grouped into families it is important that they are grouped based on a rationale that is appropriate for the EO sterilization process.

EO产品族可由相似产品的各种组合组成。例如，一个产品族可以包含只是外形不同的一系列导管或用相同材料在相同的环境下生产的各种产品。当产品划分产品族时，基于EO灭菌过程的适当性来划分产品族是重要的。

The use of product families makes the validation process simpler since all products in the family would be determined to represent an equivalent or lesser challenge to the sterilization process than the representative product or internal PCD. The product family can be represented by a worst-case product (often called the “master product”); the entire family is considered an equivalent challenge to the sterilization process, or it is represented by a product PCD (internal PCD).

由于产品族中的所有产品可能被确定，其挑战性与代表产品或内部PCD相比具有相同或更低，产品族的应用使确认过程简单化。产品族可由最坏状态产品(通常被称为‘主产品’);整个产品族认为灭菌过程有等同的挑战性，或是代表产品PCD（内部PCD）。

In addition to product families, processing categories can also be used in EO sterilization routinely once the PQ has been completed. A processing category is a collection of EO product families that can be dissimilar in the details used to establish the product family, such as material of construction or packaging, or manufacturers, but each of the EO product families within a processing category should be qualified in a common sterilization process. For example, a collection of products (intravenous sets) might constitute a product family and might be placed in a processing category that includes a separate collection of products (e.g. a family of syringes). The commonality within the processing category might be the PCD that represents the microbial challenge for those products in that group. All products within this processing category should present an equivalent or lesser challenge to the sterilization process when compared with the worst-case product, representative member, or internal PCD which is placed within the product sterile barrier system.

除产品族外，一旦PQ完成了PQ，加工组可用于日常的EO灭菌。加工组是一些EO产品族的集合，这些产品族在用于建立产品族的详细信息方面有所不同，结构或包装的材料、或生产厂家，但是，加工组内的每一个产品族在通常的灭菌过程中是合格的。例如，一个产品集合(静脉套)可能组成一个产品族，并且可能被放入包含另一个产品族(如，注射器族)的加工组中。加工组内的共同点可能是能代表组内产品微生物挑战性的

PCD。当与最坏状态产品、代表产品，或放在产品无菌屏障系统内的内部PCD比较，同一个加工组内的所有产品应呈现一个相同的或更低的灭菌过程挑战性。

The review for product equivalence can be conducted within each product family or processing category. Alternatively, a worst-case product or representative member can be selected for the qualification study. In the following paragraphs, several aspects of product evaluation are addressed.

产品等效性的评审能在每个产品族或加工组内进行。此外，可选择加工组中的最坏状态产品或代表成员用于验证研究。在下面段落，讨论了产品评估的几个问题。

D.12.5.11.2 Determination of adverse effects to product 对产品不利影响的测定

Before determining whether a candidate product or packaging system can be adopted into a product family or processing category, one should determine whether the candidate product or packaging system will remain functional and effective. A system to evaluate these aspects should be addressed by the design or change control process. Consideration should be given to functionality, integrity, stability, biocompatibility, and residuals, with special consideration given to determining the effect that the sterilization process might have on drugs that could be included in devices or components. For products that contain certain types of finished components (e.g. kits with drugs), the manufacturer should consider regulatory requirements with regard to the safety and efficacy of these components in addition to the impact the sterilization process can have on the expiry date of the products involved.

在决定一个候选的产品或包装系统能否被接纳进产品族或加工组前，首先应确定候选产品或包装系统将保留其功能和有效性。评价这些方面的系统应通过设计或变更控制过程来描述。通常需要考虑功能、完整性、稳定性、生物相溶性，以及残留物，特别要考虑灭菌过程对包含在器械或组件中的药物的影响。对于含有某些组件(如，含药的组合包)的产品来说，制造商应考虑，除了灭菌过程对涉及产品的失效期的影响外，法规关于这些组件的安全性和有效性的要求。

The EO process for which the product will be tested should constitute a representative challenge to the product and its packaging system. Documentation should address how the challenge process differs from the nominal process, and the product qualification should demonstrate that these parameters are acceptable for product acceptance.

EO过程的试验产品及其包装系统挑战性应具有代表性。记录应描述挑战过程与标称过程的不同程度，并且，产品验证应证明这些参数对产品接受性来说是可接受的。

The candidate product and its packaging should be evaluated to determine the effect on product EO residual levels, and any changes to either should be evaluated for the impact on product release.

应评估候选产品及其包装，以确定对产品EO残留水平的影响，以及评估二者的任何变化对产品放行的影响。

ISO 10993-7 should be used as guidance for making this evaluation.

评估时ISO10993-7应作为指南。

D.12.5.11.3 Determination of product design effects 产品设计影响的测定

The design of the candidate product should be carefully reviewed for any changes or differences that could present greater obstacles to EO, heat, or humidity penetration than the existing product or PCD. Examples of possible changes include longer lumens, the addition of closures, or a larger number of mated surfaces or product density.

应对候选产品进行仔细评审，与基准产品或PCD相比，是否有更阻碍EO、热或湿穿透的任何变化或区别。例如，可能的变化包括更长的管腔，闭口的增加，或更大的配合面或产品密度。

Review the product design against the original product functionality testing to ensure that the changes do not adversely affect the function of the product.

针对产品功能性试验的产品设计评审，以确保变化未影响产品的功能

NOTE, This evaluation typically does not include areas of the device that

are hermetically sealed and cannot be exposed during intended use. Examples are items such as sealed, hollow, moulded parts or sealed lumens.

注，评估通常不包括产品密封的并且使用时不暴露的区域。比如，内腔封闭的注塑件或封闭的管腔。

D.12.5.11.4 Determination of product material and characteristics effects 产品材料和特性影响的测定

The characteristics of the candidate product should be carefully examined for any differences that could potentially affect the product bioburden, such as manufacturing production methods, facilities, location, and raw material types and sources. The materials of construction should be reviewed to ensure that the product will not retain higher EO residual levels or levels that will exceed the regulated limits.

应检查可能影响产品生物负载的候选产品的任何不同特性，如，生产工艺、生产工厂、生产区域，以及原材料种类和来源。应评审构造材料，以确保产品的EO残留不会很高或超过规定的限度。

D.12.5.11.5 Determination of sterile barrier system effects 无菌屏障系统影响的测定

The sterile barrier system of the candidate product should be carefully examined for any factors that could present obstacles to EO, heat, or humidity penetration. These factors can include a decrease in porosity of the venting material, a smaller venting surface area, the occlusion of the venting area, or any other feature that would make the candidate product a greater challenge to the sterilization process than the existing product or product internal PCD. In addition, the effects of changes to the sterile barrier system on the bioburden of the product and any effects on EO residual levels should be evaluated.

应检查候选产品无菌屏障系统的阻碍EO、热或湿穿透的因素。这些因素包括透析材料透析孔的减少、小的透析面积、透析区域的封闭、或其他与基准产品或PCD相比具有

更大灭菌挑战性的特点。此外，应评估无菌屏障系统对产品生物负载的影响，以及对EO残留水平的影响。

D.12.5.11.6 Determination of load configuration effects产品装载方式影响的测定

The load configuration of the candidate product should be carefully examined for any changes that could affect the thermodynamic response to the sterilization process. These changes could include additional layers of stretch wrap, a reconfiguration of the pallet, a change in the load size, a change to the overall density of the load, or any other change that would make the candidate product a greater challenge to the sterilization process.

应检查候选产品影响灭菌过程热力学反应的装载方式的任何变化。这些变化包括缠绕膜层数的增加、托盘的重置、或装载形式的变化、装载的总体密度的变化，或其他可能使候选产品产生更大灭菌挑战性的变化。

D.12.5.11.7 Conclusions of product adoption evaluation产品通过评价的结论

If the results of the written technical review show that the candidate product and existing products or internal PCD are similar and the differences between them are determined to be insignificant or to present a lesser challenge than the currently validated product or internal PCD, then the candidate product can be adopted into the product family or processing category without further study. If AAMI TIR28:2009[26], Annex A, was used for the review, this decision would be supported by virtually all “No” answers to the questions. The rationale for this decision should be made by a sterilization specialist and should be documented. If the technical review indicates that the candidate product has the potential to be a greater challenge to the sterilization process than the currently validated product or internal PCD, then further studies are indicated. If the candidate product is determined to represent a greater challenge to the sterilization process, then it does not meet the requirements for adoption into an existing product family or processing category, and a full PQ needs to be performed. This PQ can:

如果书面的技术评审结果显示，候选产品与基准产品或内部PCD是相似的以及二者之间的差异是可以忽略不计的或比目前已验证产品的挑战性更低，那么，候选产品可以归入产品族或加工组中而不需进一步研究。如果AAMI TIR28:2009[26], Annex A用于评审，对问题的回答全部是‘No’，可以支持这个结论。这个结论的合理性应由灭菌专家来说明，并应记录。如果技术评审显示，与目前已验证的产品或内部PCD相比，候选产品可能具有更大的灭菌挑战性，那么，需要进行进一步的研究。如果确定候选产品有更大的灭菌挑战性，就不能归入基准产品族或加工组，应进行全部的PQ。这个PQ可以：

a) establish a new product family or processing category, with the candidate product as the representative product;

用候选产品作为代表产品，建立新的产品族或加工组；

b) establish a new internal PCD for the sterilization process;

给灭菌过程建立新的内部PCD；

c) establish that the candidate product is equivalent to the currently validated master product; or

建立候选产品等同于目前已验证的主产品

d) establish a new sterilization process for the candidate product.

给候选产品建立新的灭菌过程。

Annex A

(normative)

Determination of lethal rate of the sterilization process — Biological indicator/bioburden approach

灭菌过程的致死率的测定——生物指示剂/生物负载方法

A.1 General

A.1.1 This approach combines knowledge of the resistance of a biological indicator to a given sterilization process with knowledge of the bioburden population and resistance to establish the sterilization process parameters (sterilization cycle exposure time).

本方法结合了生物指示物对给定周期的抗力和生物负载与抗力方面的知识，以建立周期参数（作用时间）。

Use of the method requires that product bioburden levels shall be demonstrated to be relatively consistent over time and the resistance of the bioburden be shown to be equal to, or less resistant than the resistance of the biological indicator (see D.8.6). 使用本方法要求证明产品的生物负载水平在一定期限内保持相对稳定以及生物负载的抗力小于等于生物指示物的抗力。

The resistance of the internal PCD is demonstrated by running the sterilization cycle at graded exposure times, or by exposing graded BI populations to a single sterilization exposure time, and then determining the lethal rate (rate of inactivation through D-value calculations) when exposed to the sterilization cycle. Knowledge of the BI lethality rate and the population and relative resistance of the bioburden allows one to establish exposure time so that an SAL can be predicted.

通过逐步增加作用时间和确定周期的灭活率证明生物指示物的抗力。这一比率和生物负载的菌数及相对抗力方面的知识可用于确定灭菌时间，从而可以预测SAL。

Attention shall be given to the impact of packaging and the removal of EO from the PCD.

应注意，包装和PCD的EO残留的影响。

Guidance on this approach can be found in ISO 14161.

本方法的指南见ISO14161。

D.13.1.1 [A.1.1] This clause provides further guidance to information in Annex A and D.8 through D.9. Since the biological indicator/bioburden approach and the overkill approach use many of the same procedures, some of the text in this clause duplicates text in D.14.

本章节为附录A和D.8到D.9的信息提供进一步的指南。由于生物指示剂/生物负载法和过度杀灭法使用许多同样流程，这个章节的有些内容与D.14章节重复。

The combined biological indicator/bioburden approach is based on the use of a resistant BI or other internal PCD with a population that is equal to or greater than that of the bioburden. This method is appropriate when sufficient bioburden data are available from the bioburden monitoring program to demonstrate that the product bioburden resistance along with the population can be appropriately represented during the validation studies to deliver a 10^{-6} SAL to the product.

生物指示剂/生物负载结合法是基于抗力BI或其他内部PCD大于或等于生物负载数量的。当，在产品10^{-6}无菌保证水平的确认验证时，用来证明产品生物负载的数量与抗力具有关联性的通过生物负载检测获得的充分的生物负载数据是可用的，那么这一方法是合适的。

NOTE, This method can involve the use of a BI or other internal PCD with a population of less than 10^{6}.

注，这个方法涉及数量低于10^{6}的BI或内部PCD的使用。

The relative resistance and population of the internal PCD should be compared with the resistance and population of the product bioburden. The log reduction of the internal PCD can be used to calculate the sterility assurance level achieved for the product bioburden with the most resistance to the sterilization process.

内部PCD的孢子数与抗力的关系，应与产品生物负载数和抗力作比较。内部PCD的对数下降值能用于无菌保证水平的计算。

If this is the case, then the Spore Log Reduction (SLR) data developed in a

lethality study for the BI can be used to demonstrate the effectiveness of the process for the product. If the data are generated using an enumeration method, then the SLR can also be predicted from the survivor curve data that are generated. The user should be aware that the minimum cycle time derived from this approach is not, by itself, adequate to validate the sterilization process. Demonstration of the ability to maintain process parameters within defined limits during the proposed full cycle is necessary.

如果是这种情况，那么，在生物指示物的杀灭力研究中开发的孢子对数下降(SLR)数据可用来证明产品灭菌工艺的有效性。 如果数据是采用计数法产生的，那么，孢子对数下降值也可从产生的残存曲线数据中预测。用户应注意，从这一方法得出的最小周期时间本身来说，是不足以确认灭菌工艺。在建议的完整周期时过程参数保持在规定的极限范围内的能力证明是必需的。

If the product bioburden is tested at frequent intervals and is consistent, then a combined biological indicator/bioburden method can be used for process definition and/or MPQ.

如果产品生物负载试验是频繁的和一贯的，那么，生物指示剂/生物负载结合法能用于过程定义和/或MPQ。

Process lethality determinations: the microbiological lethality delivered to a product after exposure of the product to a particular process can be calculated based on the *D* value of a specified microorganism. Because microorganisms generally die at a rate that is approximately logarithmic for a given process, a time unit of exposure to EO gas can be found to result in the destruction of 90 % of the microorganism’s population regardless of the population size. Each of these time units is referred to as the *D*-value for the product microbiological contaminant, when exposed to the specified sterilization process.

过程杀死力确定：产品在特定过程暴露后的微生物杀死率可用微生物D值来计算，由于微生物大概以对数速率死亡，能杀灭90%的微生物为一个EO气体暴露时间单位。当暴露于特定的灭菌过程时，每个时间单位作为产品微生物污染的D值。

The *D*-value of a specified microorganism and the microbiological lethality delivered to the product when exposed to a specified sterilization process can be calculated using the results from one of two commonly used methods. The first method (enumeration) consists of an enumeration or physical count of the survivors and the second (fraction-negative) uses growth/no growth during fractional cycles.

Either of these methods can be used for Annexes A or B. *D* values can be calculated by using the results from the fractional cycles and equations described in ISO 11138-1 and ISO 14161.

特定微生物的D值和暴露于特定灭菌过程的产品微生物杀死力可用二种常用方法的一种得出的结果来计算。第一种方法(计数)由计数器和菌落计点器组成，第二种方法(部分阴性)使用短周期时的生长/未生长方法。这些方法的任何一种都可用于附录A或B。可用短周期结果来计算D值，方程在ISO11138-1和ISO14161中描述。

It might be appropriate to consider the impact of EO injection and post exposure evacuation time to provide greater accuracy in determining the lethal rate. This impact will be most significant when EO injection and post exposure times are lengthy compared to the EO exposure time, see Reference.[40]

在测定杀死率时获得更高的准确率，要考虑EO注射和暴露后去除时间。当EO注射和后暴露时间冗长地与EO暴露时间比较时，这个影响将是最明显的，见参考资料[40]。

Regardless of the method used, it is assumed that:

不管作用什么方法，前提是:

a) the microorganism population is homogeneous;

微生物数量是均衡的;

b) the process parameters are constant from run to run;

每个运行的过程参数是不变的;

c) a semi-logarithmic survivor relationship exists;

半对数存活曲线存在。

d) microorganisms that have survived the process and unexposed microorganisms respond similarly in the recovery medium;

在过程中存活的微生物与未经暴露的微生物在培养介质的响应相似。

e) all microbiological test methods (tests of sterility, enumeration, etc.) should be validated in accordance with ISO 11737-1 and 11737-2.

所有微生物试验方法(无菌试验、计数等)应按ISO11737-1和ISO11737-2的要求验证。

Enumeration: enumeration consists of exposing internal PCDs to the fractional cycle, removing the challenge and performing survivor counts on the samples or biological indicators. The survivor count can be used in developing a survivor curve and *D* value. The *D*-value is then calculated using a linear regression model.

See ISO 14161:2009.

计数由短周期暴露内部PCD、去除挑战和进行样品或BI的存活微生物计数构成，存活微生物计数可用于开发存活曲线和D值。然后，用线性回归模型计算D值。

见ISO14161：2009

Fraction-negative: fraction-negative analysis involves running sterilization cycles in which some, but not all, of the biological indicators are inactivated. This includes:

部分阴性:部分阴性分析涉及运行BI失活但并不全部失活的灭菌周期。包括:

a) Holcomb-Spearman-Karber (HSK) procedure;HSK流程

b) Limited Holcomb-Spearman-Karber (LHSK) procedure;极限HSK流程

c) Stumbo-Murphy-Cochran (SMC) procedure.SMS流程

See ISO 14161:2009.见ISO14161:2009

Sample size: the number of samples depends on the method used and whether the

samples are distributed throughout the load or concentrated in one location. Use of a single location can improve consistency of results between samples; however, it might not represent the worst case location in a chamber unless extensive mapping has been performed in each chamber with each possible load configuration.

样品大小:样品的数量取决于使用的方法，以及样品是否分布在装载的各处或集中在一个位置。单一位置的使用可提高样品间结果的一致性，然而，这样也许不能代表柜内最坏状态位置，除非，广泛的映射被用于每一柜内的每一可能装载方式。

When evaluating results, consideration needs to be given to ensure that the differences in the number of surviving microorganisms between replicate challenges are due to random variation within a population rather than a variation in exposure conditions.

当评估结果时，必须考虑到，要确保，重复挑战间的存活微生物数量的差异是在数值内随机变化的，而不是暴露条件的变化。

For further guidance on the number of biological indicators, see Table C.3. In addition, see ISO 11138-1 and ISO 14161 to ensure that the minimum number of samples is met.

BI数量的进一步指南，见表C.3。此外，见ISO11138-1和ISO14161以保证样品的最少数量。

In order to achieve the desired results, it might be necessary to shorten the post-exposure phases of the cycle.

为了获得所需的结果，缩短周期的后暴露阶段可能是必须的。

A.1.2 The conditions used for recovery of biological indicators in qualification studies, including duration of incubation, shall be established and documented. The incubation period shall take into account the possibility of delayed outgrowth of spores that have been exposed to EO. Refer to ISO 14161 for additional information on biological indicator incubation times.

应建立和文件化用于生物指示剂复活的条件，包括培养时间。培养周期应考虑到暴露于EO的孢子复活的可能性。有关生物指示剂培养时间的附加信息参考ISO14161.

D.13.1.2 [A.1.2] Information on the incubation period for biological indicators is provided in ISO 14161:2009, subclause 12.3.

ISO14161:2009,第12.3章节提供了BI培养期限的信息。

A.1.3 After time-graded exposures to EO or population-graded BIs exposed to EO, with all other parameters remaining the same, the lethality of the process can be determined by using one of the following methods:

时间递次的EO暴露或数量递次BI暴露于EO以后，在其他参数保持不变的情况下，过程的致死率可以通过使用下列方法之一来测定:

a) direct enumeration;直接计数;

b) the fraction-negative method; or部分阴性法，或

c) a combination of a) or b) above.结合实际a)或b)

NOTE The fraction-negative method uses growth/no growth data from the recovery test on the reference microorganisms after exposure to fractional gas exposure times; or to graded populations of reference microorganisms to a single fractional gas exposure time.

注：部分阴性法采用在短周期气体作用时间后PCD复活检测中有无细菌生长的方法。或测定短时间暴露于EO的微生物的数量。

D.13.1.3 [A.1.3] It is possible to combine the enumeration and fraction-negative approaches for determining lethality or *D* values. The two approaches are based on different calculation methods. Users generally select one method or the other for determining process lethality.

计数法和部分阴性法相结合来测定杀死力或D值是可能的。这二种方法是基于不同的计算方法。使用者通常选择一种方法或其他测定过程杀死力的方法。

A.2 Procedure

For additional guidance on this developmental process refer to AAMI TIR 16 and ISO 14161, both of which discuss process development in detail.

此外，开发过程的指南参考AAMI TIR 16和ISO14161，标准是均详细讨论了过程开发。

D.13.2 [A.2] Procedure 程序

The location within the product at which sterility is most difficult to achieve might include not only those areas that have reduced sterilant penetration, but also those areas that are more likely to have a significant amount of bioburden present. A review of the product should be conducted to establish an appropriate placement of the biological challenge. The review should be documented. See ISO 14161:2009, 7.2.2.

产品内无菌状态最难达到的位置不只是包括那些阻碍灭菌剂渗透的区域，也包括那些生物负载高的区域。应进行产品评审，以建立微生物挑战的适当位置。评审应记录。见 ISO 14161:2009[3]第7.2.2条

Aspects to consider are:考虑的因素：

a) the length and inside diameter of lumens, and whether or not the wall of the medical device allows diffusion of EO;

腔管的长度和内径，及医疗器械的壁是否允许EO扩散；

b) absorbency of the different parts of both the product and material;

产品和材料不同部位的吸收度；

c) weights and densities of items;

灭菌产品的重量和密度；

d) load configuration, especially for a mixed product load.

装载方式，尤其是混合产品的装载

See ISO 11138-1 and ISO 14161 to ensure that the requirement for the minimum number of samples is met.

参考ISO 11138-1 and ISO 14161，以保证最少样品数量得到满足。

ISO 14161:2009, Annex A, provides additional guidance on the application of the relationship between the BI and the product bioburden in the biological indicator/bioburden approach.

ISO14161:2009,附录A,提供了BI/生物负载方法BI和产品生物负载之间的关系的应用指南。

It is important that the internal PCD provides an equal or greater challenge than that of the bioburden located in the most inaccessible portion of the product. See D.7.1.6 for information on the development of PCDs and D.8.6 for information on determining the appropriateness of the internal PCD, placed within the sterile barrier system of the product.

内部PCD挑战性等于或大于放置于产品最难灭菌位置的生物负载是十分重要的。有关PCD设计的信息见D.7.1.6,测量放置在产品无菌屏障系统内的内部PCD适当性的信息见D.8.6。

The parameters that primarily affect lethality are exposure time, EO concentration, humidity and temperature. If an adjustment of parameters other than exposure time is made, the overall effect to the cycle should be evaluated since the adjustment might not achieve the desired result because the parameters are interrelated. For example, the result of decreasing temperature would actually increase the EO concentration and the relative humidity if no change is made to the pressure parameters.

影响杀死力的主要参数是暴露时间、EO浓度、湿度和温度。如果发生暴露时间以外的参数调整，由于参数是关联的，调整可能无法获得准确结果，应评估对周期的总体影响。例如，如果压力参数未发生变化，降低温度的结果其实相当于增加EO浓度和相对湿度；

The data obtained from process lethality studies are used to establish the minimum EO gas exposure time required for the sterilization process. If these studies are performed in a developmental chamber, caution should be taken in

directly applying this time to the sterilization process because kill curves (lethality rates or *D* values/SLRs) are specific to the process parameters, chamber load configuration, and PCD placement within packaged product within the load used for the study.

灭菌过程EO气体最低暴露时间的建立来从过程杀死力研究获得的数据。如果这些研究在研发性柜室中进行的，直接将暴露时间应用于灭菌过程应慎重，因为，杀灭曲线(杀死率或D值或SLRs)是特定于研究的过程参数、柜室装载方式、和装载内放在产品包装内PCD。

For additional information on direct enumeration and fraction negative-methods, see ISO 11138-1:2006, Annex D and ISO 14161:2009, Annex C.

关于直接计数和部分阴性法的其他信息，见ISO 11138-1:2006的附录D和ISO 14161:2009的附录C.

Annex B

(normative)资料性规范

Conservative determination of lethal rate of the sterilization process — Overkill approach

灭菌过程致死率保守性确定方法——过度杀灭法

B.1 General

B.1.1 This approach to process definition is based on the inactivation of reference microorganisms and has been widely used (see also ISO 11138-2). Sterilization processes qualified in this manner are often conservative and use a treatment that may exceed that required to achieve the specified requirements for sterility.

本过程定义方法的基础是基准微生物的灭活，本方法已得到广泛使用(see also ISO 11138-2)。采用本方法鉴定的灭菌过程通常具有保守性，所用的处理水平可能超过了达到无菌要求所需的处理水平。

Guidance on this approach can be found in ISO 14161.

D.14.1.1 [B.1.1] This clause provides further guidance to information in Annex B, and supplementary guidance to information in Clauses 8 and 9. Since the biological indicator (BI)/bioburden approach and the overkill approach use many of the same procedures, some of the text in this annex duplicates text in D.13. However, when using the cycle calculation approach, see also D.13.1.1. For further information regarding the use of the overkill approach see ISO 14161:2009, 7.2.

这个章节对附录B的信息提供进一步的指南， Clauses 8 and 9信息的补充指南。由于BI/生物负载法和过度杀灭法使用的程序大都同样，这个附录中有些文本内容在D.13中重复。然而，当使用周期计算法时，也可D.13.1.1。关于过度杀灭法使用的进一步信息见ISO 14161:2009。

The user should be aware that the minimum cycle time derived from this approach is not, by itself, adequate to validate the sterilization process. Demonstration of the ability to maintain process parameters within defined limits during the proposed full cycle is necessary.

值得注意的是，这个方法获得的最短周期时间去确认灭菌过程其本身并不充足。整周期时过程参数保持在定义的极限内的能力的记录是必须的。

B.1.2 Conservative process definition requires use of either of the approaches given in a) and b) below.

保守性过程定义需采用以下途径a）或b）之一：

a) Half-cycle approach: a total of three consecutive experiments resulting in total inactivation of the biological indicators (with a population of not less than 10^6 and, where appropriate, placed within a PCD) shall be performed in order to confirm the minimum exposure time. The specified exposure time for the sterilization process shall be at least double this minimum time. A fractional cycle of short duration from which BI survivors can be recovered shall also be run to demonstrate the adequacy of the

recovery technique for BIs exposed to EO gas.

半周期途径：应进行总共三次连续的试验，结果为灭活全部的生物指示物（PCD菌落数不少于10^6），以确认最小作用时间。规定的作用时间应至少为此最小时间的两倍。同时应运行有存活微生物的短时间周期，以证明存活技术的适宜性。

NOTE This short cycle can also be used to demonstrate the relative resistance of Biological Indicator, PCD and product bioburden.

这个短周期也可用于证明BI、PCD和产品生物负载的相对抗力。

b) Cycle calculation approach: The routine processing parameters that deliver minimally a 12 SLR of the biological indicator shall be established using one of the methods described in A.1.3. The number of cycles is dictated by the method used.

周期计算法：使用A.3描述的方法之一，确定生物指示物孢子对数降低值至少为12SLR的常规处理参数。根据所用的方法确定周期的次数。

D.14.1.2 [B.1.2] Two methods are commonly used in this approach.

二种方法常用于这个途径。

Half cycle approach: Due to its relative ease of use and the conservative SAL obtained, medical device manufacturers and health care facilities commonly use this method which is to demonstrate total inactivation of the 10^6 challenge BIs at a half-cycle exposure time. When this exposure time is doubled, a minimum 12 SLR is delivered during EO exposure. This approach will lead to a process delivering considerably more than 12 SLR.

半周期途径:由于这个方法相对容易，并可获得保守的SAL，医疗器械制造商和医疗保健机构通常使用这个用来证明半周期暴露时间10^6微生物的全部失活的方法。当这个暴露时间的二倍时，EO暴露时至少可获得12 SLR。这个途径将导致高于12个SLR。

Cycle Calculation: This method consists of exposing internal PCDs to the experimental cycle, removing the challenge and testing for survivors. This testing can be conducted by using a fraction-negative technique or by

performing viable microbial counts on the samples or challenge indicators. This information can be used to calculate the cycle necessary to deliver the defined SAL for the product. See ISO 14161:2009.

周期计算:这个方法由在实验周期中暴露内部PCD、去除挑战和存活试验组成。这个试验可以通过使用部分阴性技术来进行或通过样品或挑战指示剂上活的微生物数量来执行。这个信息可用于计算定义SAL的周期。

When using the Stumbo-Murphy-Cochran procedure and the Overkill Cycle Calculation approach, the recommended number of BI/PCDs can be based on the product volume to be sterilized with a minimum of 10, see Reference [38] and C.3. The sample set exposed at zero time should be exposed to all stages of the experimental cycle prior to sterilant injection.

当使用SMC流程和过度杀灭周期计算途径时，至少使用10个BI/PCD。0时间暴露的样品应暴露至灭菌剂注入前。

B.1.3 The conditions used for recovery of biological indicators in qualification studies shall be established and documented. The incubation period shall take into account the possibility of delayed outgrowth of spores that have been exposed to EO.

确认中用于生物指示物复活的条件，包括培养时间，应予以确定并形成文件。培养时间应考虑经暴露于EO的芽孢延迟生长的可能性。

Further guidance on the biological indicator incubation times can be found in ISO 14161.

有关BI的培养时间在ISO14161中有进一步指南。

D.14.1.3 [B.1.3] Information on the incubation period for biological indicators is provided in ISO 14161:2009, 12.3.

有关BI的培养期限在ISO14161：2009的12.3中有进一步指南。

B.1.4 The resistance of the product bioburden shall be shown to be such that, total inactivation time of the product bioburden is less than the total

inactivation time of the product BI (internal PCD).

产品生物负载的抗力应显示，产品生物负载的全部失活时间小于产品PCD(内部PCD)的失活时间。

D.14.1.4 [B.1.4] The appropriateness of the BI relative to the bioburden inactivation time can be demonstrated by a test of sterility, either before or during process definition using a fractional-cycle of the appropriate exposure time.

采用一个适当暴露时间的短周期的工艺定义前或工艺定义期间的无菌状态试验，可证明生物指示物相对生物装载抗力的适宜性。

B.2 Procedure

B.2.1 Create a challenge to the sterilization process, PCD, comprising a known number of microorganisms with known resistance to EO, by placing biological indicators in the product or inoculating product at locations where sterilizing conditions are most difficult to achieve. If the location(s) of the microbiological challenge is other than the most difficult-to-sterilize within the product, its relationship to the most difficult location(s) shall be established. 通过将微生物指示剂放置或接种于产品的最难灭菌的部位的方法，制作一个已知EO抗力的微生物的数量的用于挑战过程过程的PCD，如果监测位置不是最难灭菌的位置，应确定其与最难灭菌位置的关系。

D.14.2.1 [B.2.1] Internal PCDs placed within the product sterile barrier system can be used for this method. If used, they should provide at least as great a challenge to sterilization process as the product they represent. The challenge of the internal PCD to the sterilization process should be at least that of the bioburden located in the most inaccessible portion of the product (See D.7.1.6 and D.8.6). See 7.1.6 for information on the development of PCDs and 8.6 and D.8.6 for information on determining the appropriateness of the internal PCD for the product microbiological challenge.

这一方法可使用放置在产品无菌屏障系统内的内部PCD，如果使用，其对灭菌工艺的

抗力至少与所代表的产品一致。 内部PCD的对灭菌过程的挑战性至少与放置在产品最闭塞部位的生物负载一致。详见 7.1.6 关于PCD的设计和 8.6 关于确定内部PCD对于产品微生物挑战的适合性的信息。

B.2.2 Use of a PCD that has demonstrated an equivalent or greater microbiological resistance to the sterilization process than the product meets this requirement. Attention must be given to the impact of packaging and the removal of sterilant from the PCD.

已证明微生物抗力至少等于产品的PCD的使用满足要求。必须注意包装和PCD内灭菌剂的影响。

D.14.2.2 [B.2.2] The location within the product at which sterility is most difficult to achieve might include not only those areas that have reduced sterilant penetration, but also those areas that are more likely to have a significant amount of bioburden present.

产品内最难达到无菌状态的部位不仅是包括那些灭菌剂渗透减少的区域，还可以是那些有明显生物负载量的区域。

Aspects to consider are:

考虑的因素是:

a) the length and inside diameter of lumens, and whether or not the wall of the medical device allows diffusion of EO;

腔管的长度和内径，及医疗器械的壁是否允许EO扩散;

b) absorbency of the different parts of both the product and material;

产品和材料不同部位的吸收度;

c) weights and densities of items;

灭菌灭菌的重量和密度;

d) load configuration, especially for a mixed product load.

装载方式，尤其是混合产品装载。

Health care considerations: To demonstrate adequate penetration of EO, humidity and heat into product, a PCD should be chosen for routine monitoring and validation of the EO sterilization process. The resistance of the PCD to EO should be shown to be equal to or greater than the resistance of the bioburden of product to be sterilized at the most difficult to sterilize location on the product.

B.2.3 Place the PCD (in accordance with B.2.1 and B.2.2) within or on the sterilization load as appropriate. 将PCD放置于产品中或产品上。

B.2.4 Expose the sterilization load to EO under conditions designed to deliver less lethality than the specified sterilization process.

D.14.2.4 [B.2.4] Obtaining microbial enumeration data or fractional kill data requires exposing the microbial challenge to less lethality than is present in the normal production cycle. This is usually accomplished by reducing the exposure time while holding all other parameters either constant at nominal conditions, or at selected minimum acceptable processing conditions. Utilizing the allowed minimum process temperature for the enumeration study ensures the required lethality is obtained when operating within the specified temperature range.

要获得微生物计数数据或部分杀灭力数据，需将生物监测器材曝露在比正常生产周期杀灭力小的条件下。要达到上述条件，通常是减少作用时间，同时保持所有其它参数在正常条件下不变，或在所选的最低允许处理条件下。利用计数研究所允许的最低处理温度可保证在规定的温度范围内运行时获得要求的杀灭力。

The parameters that primarily affect lethality are exposure time, EO concentration, humidity, and temperature. If an adjustment of parameters other than exposure time is made, the overall effect to the cycle should be evaluated since the adjustment might not achieve the desired result because the parameters are interrelated. For example, the result of decreasing temperature would actually increase EO concentration and relative humidity if no change is made to the steam injection pressure and the EO injection pressure rise.

影响杀灭力的主要参数为曝露时间、EO 浓度、湿度和温度。除曝露时间外，调节参数后就应评估总体灭菌效力。因为各参数的相关性，参数调节可能会导致无法达到要求的灭菌结果。如：降低温度而不改变气体压力，实际上增加了EO 浓度。

B.2.5 For the cycle calculation approach, if the inactivation of a known number of microorganisms has been confirmed according to A.1.3, determine the extent of treatment for the sterilization process by extrapolation to a known predicted probability of a surviving microorganism, taking account of the required SAL.

如果已知微生物数量的灭活已根据A.3进行确认，推断已知的微生物存活预期可能性，并考虑所需的SAL，确定灭菌过程处理的范围。

D.14.2.5 [B.2.5] SLRs can be calculated using the results of fractional cycles. If there are no surviving internal PCDs, a worst-case estimate of the SLR can be obtained by running the calculation with one assumed survivor.

用附录A中部分周期、公式及样本结果来计算 SLR值。

Regardless of the method used, it is assumed that:

无论何种方法，都假定：

a) the organism population is homogeneous;

微生物总菌数是均匀一致的；

b) the process parameters (except gas exposure time) are constant from run to run;

每一回的工艺参数 (除气体曝露时间外)是恒定的；

c) a semi-logarithmic survivor relationship exists;

存在半对数存活关系；

d) exposed and unexposed organisms respond similarly in the recovery medium.

在恢复培养基中曝露和非曝露微生物的反应是相似的。

Annex C

(informative)规范性附录

Temperature sensors, RH sensors and biological indicator Numbers温度传感器、湿度传感器和生物指示剂数量

C.1 Temperature sensors温度传感器

It is recommended to use one sensor per 2,5 m^3 during OQ to establish a thermal map of the room or chamber that captures potential hot or cold locations. Therefore, monitoring should include more than one plane and locations near doors.

OQ时建议每2.5 m^3一个传感器,以建立室或柜热分布图来捕捉潜在的热点或冷点。然而，监视应包括多于一个平面和门附近的点。

For PQ, one temperature sensor is required per cubic metre of product volume. The minimum number of temperature sensors is three. For PQ, humidity sensors should be placed within the packaging (where possible) within the load. This can be achieved by placing the sensor within the sterile barrier system or amongst the unit packages.

PQ时，每立方产品体积要求一个温度传感器，但每柜不得少于3个。PQ时，湿度传感器应放在装载内的包装内。这可以通过把传感器放在无菌屏障系统内或单位包装中来达到。

The result of the calculation should be rounded to the next higher number.

计算的结果应接近数量大的。

Table C.1 provides guidance for determining the number of temperature sensors.

表C.1为确定温度传感器的数量提供了指南。

Table C.1 — Minimum recommended number of temperature sensors 温度传感器最少数量

Volume m^3	Number for OQ (usable chamber/room volume) 柜室可用体积			Number for PQ (product load volume) 产品装载体积		
	Preconditioning 预处理	Conditioning/ sterilization 处理/灭菌	Aeration 通风	Preconditioning 预处理	Conditioning/ sterilization 处理/灭菌	Aeration 通风
≤ 1	3			3		
10	4			10		
15	6			15		
20	8			20		
25	10			25		
30	12			30		
35	14			35		
40	16			40		
50	20			50		
100	40			100		

EXAMPLE During OQ of a preconditioning room with a usable chamber volume of 70 m^3: 70/2,5 = 28.

例，OQ时，可用柜室体积70 m^3的预处理间的温度传感器数：70/2,5 = 28

EXAMPLE During PQ with a product load volume of 2 m^3: 2/1 = 2. The number of sensors to use is at least three (the minimum number of sensors to use).

例，PQ时，2 m^3的产品装载体积：2/1 = 2,但传感器至少用3个。

C.2 Humidity sensors 湿度传感器

The recommendation is to use one sensor per 2,5 m^3 to establish a humidity map of the area or product that captures potential variability in the humidity levels. The minimum number of sensors is two.

建议每2.5 m^3一个传感器,以建立区或产品湿度分布图来捕捉潜在的湿度差异。湿度传感器的最少使用量是2个。

The result of the calculation should be rounded to the next higher number.

计算的结果应接近大的数字。

For PQ, humidity sensors should be placed within the packaging (where possible) within the load. This can be achieved by placing the sensor within the sterile barrier system or amongst the unit packages.

PQ时，湿度传感器应放在装载内的包装内。这可以通过把传感器放在无菌屏障系统内

或单位包装中来达到。

Table C.2 provides guidance for determining the number of humidity sensors.

表C.2为确定温度传感器的数量提供了指南。

Table C.2 — Minimum recommended number of humidity sensors

Volume m^3	Number for OQ (usable chamber/room volume)			Number for PQ (product load volume)		
	Preconditioning	Conditioning/ sterilization	Aeration	Preconditioning	Conditioning/ sterilization	Aeration
≤ 1	2			2		
10	4			4		
15	6			6		
20	8			8		
25	10		N/A	10		N/A
30	12			12		
35	14			14		
40	16			16		
50	20			20		
100	40			40		

EXAMPLE 1 During OQ for a usable chamber volume of 6 m^3: 6/2,5 = 2,4. The number of sensors to use is at least three.

例1，OQ时，6 m^3可用体积的柜室：6/2,5 = 2.4,但至少是3个。

EXAMPLE 2 During PQ for a product volume of 60 m^3: 60/2,5 = 24. The number of sensors to use is at least 24.

例2，PQ时，60 m^3产品体积：60/2,5 = 24,至少使用24个湿度传感器。

C.3 Biological Indicators 生物指示剂BI

The minimum recommended number of BI/PCDs to use is as follows:

BI/PCD最少使用量如下：

a) For MPQ with a product load volume of up to 10 m^3, use three BIs per m^3 of product volume, with a minimum of five BIs.

MPQ时，产品装载体积不超过10 m^3的，3个BI/ m^3，但至少用5个BI。

b) For MPQ with a product load volume above 10 m^3, use one additional BI per additional m^3 beyond 10m^3.

MPQ时，产品装载体积超过10 m^3的，再增加1个BI/1m^3。

If BIs are used for routine control use half the number of BIs used during MPQ up to a maximum of 30.

日常使用BI数是MPQ时的一半，但最多是30个。

The result of the calculation should be rounded to the next higher number.

计算的结果应接近大的数字。

Table C.3 provides guidance for determining the number of BI/PCDs.

表C.3为确定BI/PCD的数量提供了指南。

The actual number of BI/PCDs to be used will depend on:

BI/PCD实际使用量取决于:

a) microbiological qualification method chosen (see Annex A or Annex B);

选择的微生物验证的方法(见附录A或附录B)

b) product volume;产品体积

c) type of chamber (developmental vs. production).柜室类型(研发性还是生产性)

When using the Stumbo-Murphy-Cochran procedure and the Overkill Cycle Calculation approach the recommended number of BI/PCDs can be based on the product volume to be sterilized. When this approach is being used a minimum quantity of 10 BI/PCD’s are indicated, see Reference [38].

当应用SMC流程和过度杀灭循环计算途径时，BI/PCD是按灭菌产品体积计算的。当应用这个途径时，至少用10个BI/PCD，见参考资料38。

Table C.3 — Examples of minimum recommended number of BI/PCDs

Product load volume m^3 产品装载体积	MPQ	Routine control (if used) 日常控制
≤ 1	5	3
10	30	15
15	35	18
20	40	20
25	45	23
30	50	25
35	55	28
40	60	30
50	70	30
100	120	30

EXAMPLE 1 For product load volume of 3 m^3: 3 × 3 = 9. The number of BIs to use is at least nine for MPQ. For routine control: 9/2 = 4,5. The number of BIs is at least five.

例1，3 m^3产品装载：3 × 3 = 9。MPQ时，BI/PCD至少使用9个。日常控制：9/2 = 4.5，至少使用5个。

EXAMPLE 2 For a product load volume of 18 m^3: 10 × 3 + (18 − 10) × 1 = 38. The number of BIs to use is at least 38 for MPQ. For routine control: 38/2 = 19. The number of BIs is at least 19.

例2，18 m^3产品装载：10 × 3 + (18 − 10) × 1 = 38，MPQ时，至少用38个BI。日常控制：38/2 = 19，至少用19个BI.

Annex E

(normative)规范性附录

Single Lot Release单批放行

E.1 General通则

This annex specifies the requirements for the release of product from a sterilization process where there is only sufficient product to comprise a single sterilization load, for example, during research and development of new product or for clinical trial product.

本附录规定了产品量只够用于一次产品装载的灭菌过程的产品放行要求，例如，新产品的研究和开发阶段或临床试验产品。

NOTE Attention is drawn to the possible existence of national or regional regulations for clinical product. Where such regulations are in force, the requirements of these regulations should be followed.

注，需注意的是，国家或地区的法规可能对临床产品另有规定。应执行有效的法规。

E.2 Procedure程序

E.2.1 Assess the packaged product to determine if it can be assigned to an existing product family for sterilization purposes. This assessment considers product composition, design, packaging, bioburden and load density. The outcome of this assessment, including the rationale for decisions reached, is documented.

评估已包装产品是否可以归入目前的灭菌产品族，评估考虑产品的组成、设计、包装、生物负载和装载密度。评估的结果，包括得出结论的理由，应记录。

E.2.2 If the packaged product can be assigned to an existing product family refer to 12.5.2 and D.12.5.2.

已包装产品能否归入目前的产品族，参考12.5.2 和 D.12.5.2。

E.2.3 Where there is no existing product family(ies), or where packaged product cannot be assigned to an existing product family:

没有现有的产品族，或已包装产品不能归入现有的产品族：

a) Randomly select samples from the batch and determine the average bioburden of the batch in accordance with ISO 11737-1.

从这批次中随机抽取样品，按ISO11737-1的要求检测这批次的平均生物负载。

b) Distribute product test of sterility samples and internal PCDs that are located within packaged product throughout the sterilization load, including locations where sterilizing conditions are most difficult to achieve. Place

external PCDs (if used) on the load in defined locations. The PCD contains BIs that comply with ISO 11138-2:2006, Clause 5 and 9.5.

出具产置在灭菌装载各处的包装产品内的样品产品和内部PCD的无菌试验，包括最难灭菌的点，将外部PCD放在规定点的装载上。PCD包含的BI应符合ISO11138-2:2006中5和9.5条款的要求

NOTE The locations used should include those used for temperature monitoring.

这些点应包括温度监视的点。

c) Expose the sterilization load to a fractional EO gas exposure cycle at minimum process parameters estimated to deliver an SAL of $< 10^{-1}$ for product and a 7 to 8 log10 reduction in the PCD.

将灭菌产品暴露于估计可使产品SAL小于10^{-1}和PCD降低7～8对数的低限过程参数短周期中

d) Remove internal PCDs, external PCDs (if used) and product test samples from the load and subject to tests of sterility in accordance with ISO 11737-2.

从装载中取出内部PCD、外部PCD和试验产品样品，按ISO11737-2要求进行无菌试验。

NOTE If comparative resistance of the internal PCD versus product bioburden has previously been assessed using a fractional cycle of shorter duration than that of the fractional cycle in E.2.3 c), and there have been no positive test results from the product test of sterility samples, then it is not necessary to perform the test of sterility for product test samples exposed to the fractional cycle in E.2.3 c).

注，如果事先通过用比E.2.3c）的短周期更短时间的短期周期，已评估产品生物负载与内部PCD的抗力比较，并且样品产品的无菌试验无阳性的，那么，E.2.3c）中的短周期时不需要进行样品的产品无菌试验。

e) Aerate and re-equilibrate the load to ambient conditions. The aeration period is sufficient to allow EO residues to dissipate to a level that will not adversely affect new PCDs in the full exposure sterilization cycle (see

f) and g) below).

将装载通风至与环境条件一致。通风时间应足以使残留的EO不会在全灭菌周期中对新PCD造成不利的影响[见下面的f)和g)]

f) Distribute new internal PCDs that are located within packaged product throughout the sterilization load, including locations where sterilizing conditions are most difficult to achieve. Place external PCDs (if used) on the load in defined locations.

发布在灭菌装载各处的，包括灭菌条件最难到达的点，放于包装产品内的新的内部PCD。将外部PCD放在规定点的装载上。

NOTE The locations used should include those used for temperature monitoring.

注，这些点应包括那些温度监视点。

g) Process the same load by exposing it to a second sterilization cycle at nominal process parameters and where the specified exposure time is at least double that of the fractional cycle in c) above (this is a full cycle).

将同一装载用标称的过程参数进行第二次灭菌，其暴露时间至少是c)中的短周期的2倍以上(这是整周期)。

h) Remove external PCDs (if used) and internal PCDs from the reprocessed load and subject to tests of sterility.

从重新灭菌装载中取出外部PCD和内部PCD，并进行无菌试验。

E.2.4 The sterilization load can be released from sterilization if the following requirements are met:

如果能满足下列要求，灭菌产品可以放行:

a) the product bioburden presents less of a challenge to the sterilization process than the biological indicator used in the external PCDs (if used) and internal PCDs;

产品生物负载的对灭菌过程的挑战性低于外部PCD(如使用)和内部PCD的BI。

b) the process parameters for the fractional cycle comply with the process specification;

短周期的过程参数符合过程规范。

c) the load has been reprocessed by exposure to a full sterilization cycle at nominal process parameters where the specified exposure time was at least double that of the fractional cycle in E.2.3 c);

装载用标称的过程参数进行重新灭菌，其暴露时间至少是c)中的短周期的2倍以上(这是整周期)。

d) the process parameters for the full sterilization cycle comply with the process specification;

整周期的过程参数符合过程规范。

e) confirmation of no growth of the test microorganisms from external PCDs (if used) and internal PCDs exposed to the fractional sterilization cycle;

短周期的内部PCD和外部PCD的微生物试验无菌生长。

f) confirmation of no positive result growth from product test of sterility samples exposed to the fractional sterilization cycle;

短周期的样品的产品无菌试验无阳性。

NOTE If comparative resistance of the internal PCD versus product bioburden has previously been assessed using a fractional cycle of shorter duration than that of the fractional cycle in E.2.3 c), and there have been no positive test results from the product test of sterility samples, then it is not necessary to perform the test of sterility for product test samples exposed to the fractional cycle in E.2.3 c).

注，如果事先通过用比E.2.3c）的短周期更短时间的短期周期，已评估产品生物负载与内部PCD的抗力比较，并且样品产品的无菌试验无阳性的，那么，E.2.3c）中的短周期时不需要进行样品的产品无菌试验。

g) confirmation of no growth of the test microorganisms from PCDs exposed to the full sterilization cycle;

整周期的PCD无微生物生长。

h) product functionality, stability and package integrity comply with requirements after exposure to the full sterilization cycle;

产品的性能、稳定性和包装完整性符合整周期后要求。

i) confirmation that product EO residue levels comply with the requirements of ISO 10993-7 after product has been exposed to both the fractional and the full sterilization cycles; and

产品经短周期和整周期后，其EO残留符合ISO10993-7的要求。并

j) all quality and regulatory requirements have been met.

满足全部的质量和法规要求。

NOTE Information and data generated from this approach can be used retrospectively to support future validation of the sterilization process.

注，从这一途径产生的信息和数据可用于支持将来灭菌过程的确认。