Medical Device Manufacturing Co;Ltd

医疗器械有限公司

VALIDATION REPORT 验证报告	
Product Family Half Cycles Qualification in current Sterilizer 产品族在现有灭菌柜的半周期确认	
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目录

1. 验证目标 Validation Objective

1.1.此次半周期确认的目的是证实及用文件记录在现有的灭菌柜内采用的预先设定的灭菌循环，通过实施灭菌微生物杀灭（MPQ）及物理性研究（PPQ）能够实现现有产品族的无菌保证水平 10^{-6}。此方案的设计持续符合 ISO 11135:2014-医疗产品灭菌-环氧乙烷-医疗器械灭菌过程的发展，验证及常规控制的要求。

The purpose of this Half Cycles Qualification is to demonstrate and document the attainment of a minimum Sterility Assurance Level of 10^{-6} for the sterilization of exiting product family in existing EO Sterilization Chamber through the execution of sterilization microbiological lethality studies (MPQ) and physical studies (PPQ) using predetermined sterilization cycle.This protocol is designed to be consistent with ISO 11135:2014 Sterilization of health care products - Ethylene oxide-Requirements for development, validation and routine control of a sterilization process for medical devices.

2. 报告总结 Report Conclusions

2.1.证实 Have demonstrated that：

2.1.1. 通过半周期法确认在所推荐的灭菌过程参数内达到规定的产品可接受无菌保证水平 10^{-6}。

The specified acceptance criteria (SAL 10^{-6}) are met for the duration of the proposed process specification through half cycle approach.

2.1.2. 所有来自 IPCDs 的 BI 全部杀死，来自 EPCDs 的 BI 部分存活可以接受。

All BIs from IPCDs showed total inactivated and partial BIs from EPCDs showed growth is acceptable.

2.2.在现有灭菌柜用于此次半周期确认的产品为模拟最具挑战性的模拟装载， 适用于以下产品。

The half cycle runs were conducted in existing EO sterilization chamber with dunnage load simulating the most challenging routine load were used in this half cycle qualification, and applicable for the products given below:

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序号 No.	代码 Code	产品描述 description	产品名称 Name	外箱尺寸 dimension(cm)	每箱数量 Quantity per box(pcs)	包装重量/箱 Weight/box (kg)	灭菌箱数/层数 Boxes/layers	产品体积 Volume(m^3)	密度 density (kg/m^3)
1	JP-2186	硅胶圆形开槽管 10Fr 不带引导针（粘接）JP CHANNEL DRAIN 10FR, FULL FLUTES	Silicone round drain, full channels without trocar	47*36*25	80	1.3	60/3	0.042	30.952
2	JP-2187	硅胶圆形开槽管 10Fr 带引导针（粘接）JP CHAN DRN SIL RND 10FR FULL W/TRO	Silicone round drain, full channels with trocar	47*36*25	80	2.0	60/3	0.042	47.619
3	JP-2188	硅胶圆形开槽管 15Fr 不带引导针（粘接）JP CHANNEL DRAIN 15FR, FULL FLUTES	Silicone round drain, full channels without trocar	47*29*47	80	1.8	60/3	0.064	28.125
4	JP-2189	硅胶圆形开槽管 15Fr 带引导针（粘接）JP CHAN DRN SIL RND 15FR FULL W/TRO	Silicone round drain, full channels with trocar	47*29*47	80	3.8	60/3	0.064	59.375
5	JP-2190	硅胶圆形开槽管 19Fr 不带引导针（粘接）JP CHANNEL DRAIN 19FR, FULL FLUTES	Silicone round drain, full channels without trocar	47*29*47	80	2.1	60/3	0.064	32.813
6	JP-2191	硅胶圆形开槽管 19Fr 带引导针（粘接）JP CHAN DRN SIL RND 19FR FULL W/TRO	Silicone round drain, full channels with trocar	47*29*47	80	4.1	60/3	0.064	64.063
7	JP-2210	硅胶扁平开槽管 7mm 不带引导针 3/4JP CHANNEL DRAIN 7MM, 3/4 FLUTES	Silicone flat drain without trocar	47*36*25	80	2.1	60/3	0.042	50.000

8	JP-2211	硅胶扁平开槽管 7mm 不带引导针 全开槽 JP CHANNEL DRAIN 7MM, FULL FLUTES	Silicone flat drain without trocar	47*36*25	80	1.7	60/3	0.042	40.476
9	JP-2212	硅胶扁平开槽管 7mm 带引导针 全开槽 JP CHAN DRN SIL FLT 7MM FULL W/TRO	Silicone flat drain with trocar	47*36*25	80	3.7	60/3	0.042	88.095
10	JP-2213	硅胶扁平开槽管 10mm 不带引导针 3/4JP CHANNEL DRAIN 10MM, 3/4 FLUTES	Silicone flat drain without trocar	47*36*25	80	2.3	60/3	0.042	54.762
11	JP-2214	硅胶扁平开槽管 10mm 不带引导针 全开槽 JP CHANNEL DRAIN 10MM, FULL FLUTES	Silicone flat drain without trocar	47*36*25	80	2.1	60/3	0.042	50.000
12	JP-2215	硅胶扁平开槽管 10mm 带引导针 全开槽 JP CHAN DRN SIL FLT 10MM FULL W/TRO	Silicone flat drain with trocar	47*36*25	80	3.8	60/3	0.042	90.476
13	JP-2216	硅胶扁平开槽管 7mm 带引导针 3/4 JP CHAN DRN SIL FLT 7MM 3/4 W/TRO	Silicone flat drain with trocar	47*36*25	80	3.9	60/3	0.042	92.857
14	JP-2217	硅胶扁平开槽管 10mm 带引导针 3/4 JP CHAN DRN SIL FLT 10MM 3/4 W/TRO	Silicone flat drain with trocar	47*36*25	80	4.0	60/3	0.042	95.238
15	JP-2221	硅胶圆形开槽管 10Fr 带引导针 3/4 （粘接） JP CHAN DRN SIL RND 10FR 3/4 W/TRO	Silicone round drain, 3/4 channels with trocar	47*36*25	80	2.1	60/3	0.042	50.000

16	JP-2223	硅胶圆形开槽管 15Fr 带引导针 3/4（粘接）JP CHAN DRN SIL RND 15FR 3/4 W/TRO	Silicone round drain, 3/4 channels with trocar	47*29*47	80	4.0	60/3	0.064	62.500
17	JP-2225	硅胶圆形开槽管 19Fr 带引导针 3/4（粘接）JP CHAN DRN SIL RND 19FR 3/4 W/TRO	Silicone round drain, 3/4 channels with trocar	47*29*47	80	4.1	60/3	0.064	64.063
18	JP-2226	硅胶圆形开槽管 10Fr 不带引导针 JP CHANNEL DRAIN 10FR HUBLESS	Hubless silicone round drain without trocar	47*36*25	80	1.2	60/3	0.042	28.571
19	JP-2227	硅胶圆形开槽管 10Fr 带引导针 JP CHANNEL DRAIN 10FR HUBLESS	Hubless silicone round drain with trocar	47*36*25	80	2.0	60/3	0.042	47.619
20	JP-2228	硅胶圆形开槽管 15Fr 不带引导针 JP CHANNEL DRAIN 15FR HUBLESS	Hubless silicone round drain without trocar	47*29*47	80	2.1	60/3	0.064	32.813
21	JP-2229	硅胶圆形开槽管 15Fr 带引导针 JP CHAN DRN SIL HUBLESS 15FR W/TRO	Hubless silicone round drain with trocar	47*29*47	80	3.9	60/3	0.064	60.938
22	JP-2230	硅胶圆形开槽管 19Fr 不带引导针 JP CHANNEL DRAIN, 19FR HUBLESS	Hubless silicone round drain without trocar	47*29*47	80	3.0	60/3	0.064	46.875
23	JP-2231	硅胶圆形开槽管 19Fr 带引导针 JP CHAN DRN SIL HUBLESS 19FR W/TRO	Hubless silicone round drain with trocar	47*29*47	80	5.8	60/3	0.064	90.625

24	JP-2232	硅胶圆形开槽管 19Fr 带可弯曲引导针 JP CHAN DRN SIL HUBLES 19FR BND TRO	Hubless silicone round drain with bendable trocar	47*29*47	80	5.6	60/3	0.064	87.500
25	JP-2233	硅胶圆形开槽管 15Fr 带可弯曲引导针 JP CHAN DRN SIL HUBLES 15FR BND TRO	Hubless silicone round drain with bendable trocar	47*29*47	80	3.7	60/3	0.064	57.813
26	JP-2234	硅胶圆形开槽管 24Fr 带引导针 JP CHANNEL DRAIN, 24FR HUBLESS	Hubless silicone round drain with trocar, 43" total length	47*29*47	80	9.1	60/3	0.064	142.188
27	JP-2290	硅胶圆形开槽管 28Fr 不带引导针 CHANNEL DRAIN, 28FR, HUBLESS	Hubless silicone round drain without trocar, 43" total length	47*29*47	80	5.07	60/3	0.064	79.219
28	JP-2292	硅胶圆形开槽管 32Fr 不带引导针 CHANNEL DRAIN, 32FR, HUBLESS	Hubless silicone round drain without trocar, 43" total length	47*29*47	80	6.57	60/3	0.064	102.656

3. 实施概述 Execution Summary

3.1. 前提步骤 Prerequisite Steps

3.1.1. 在半周期确认活动实施前，确认现有灭菌柜的安装确认及运行确认报告，相关报告已存档。

Verification of the IQ and OQ documentation of existing chamber had been done prior to the half cycle qualification, the documents were archived.

3.1.2. 相关人员的培训已实施，培训记录见附录 1。

Training of the half cycle qualification runs was conducted for all relevant personnel involved and the training record see attachment 1.

3.1.3. 核实温湿度无线探头，安装于灭菌柜上的温湿度，压力传感器及其他辅助设施的计量仪表的校验记录是否符合接受要求，计量仪表校验状态见仪表校验清单，符合接受要求。仪表校验状态记录见附录 2。

All calibration records/results of the temperature/ relative humidity data loggers, the temperature,RH sensors & pressure transmitter fitted to the sterilization chamber and other measurement instruments associated with the ancillary equipment were reviewed for acceptance. The calibration status for each equipment was identified in the equipment calibration list and was found to be acceptable. The record of equipment calibration status is presented in attachment 2.

3.1.4. 核实了设备维护的状态。所有的设备均依照灭菌设备维护程序规定的时间表进行维护，并用文件记录维护活动， 维护记录存档。

The status of equipment maintenance was also reviewed. All identified equipment was conducted according to the time schedule. The maintenance activities were documented and the records were archived in files.

3.2. 装载 Load

3.2.1. 完整的模拟装载(满载）用于此次半周期循环确认，产品装载体积 4.1 m^3。

The complete dunnage load (full load) had been used for this half cycle qualification . The product load volume as derived in protocol is 4.1 m^3.

3.2.2. 灭菌柜内产品的装载，内置挑战装置，外置挑战装置，无线温湿度探头的放置参考验

证方案附录 2。

The load configuration in the sterilization chamber, and the placement of IPCDs, EPCDs,and data loggers (temperature and humidity sensors) in the load were carried out according to attachment 2 of the protocol.

3.3.过程挑战装置 PCDs

3.3.1. 用于此次半周期确认的内置挑战装置采用产品产品硅胶圆形开槽管 15Fr 带引导针 3/4(粘接)，其制备参考验证方案要求进行。

Internal PCDs (IPCD - JP CHAN DRN SIL RND 15FR 3/4 W/TRO) were used in this half cycle qualification. They were prepared according to the requirements of the protocol.

3.3.2. 内置挑战装置枯草芽孢杆菌，平均菌落数为≥1.0 × 10^6/条，D 值在 54°C ≥2.5 分钟，符合验证方案的要求。

The IPCDs were inoculated with biological indicator (Bacillus atrophaeus). The average spore concentration was ≥1.0 × 10^6/strip and the D value of the BI was ≥2.5 minutes at 54°C which met the acceptance criteria as defined in the of the protocol.

3.3.3. 外置挑战装置也同样用于半周期确认，其制备与要求相一致。

EPCDs were used in this half cycle qualification runs, the preparation is same as requested.

3.3.4. 此次半周期确认的半周期所用的内置挑战装置数量为 18 个,外置挑战装置 18 个。

A total of 18 units IPCD and 18 units EPCD for half cycle runs were used in this half cycle qualification runs.

3.4.装载条件 Load Condition

产品装载在进行半周期循环前，需移入冷库冷冻至少 12h,模拟最恶劣的条件。

The validation load needs be transferred to the the freezer to storage for at least 12h simulating the worst case condition before half cycle runs.

3.5.产品装载将植入温湿度无线探头，内置过程挑战装,外置过程挑战装置。

The load will be seeded with temperature and humidity data loggers, IPCDs,EPCDs, all IPCDs and sensors will be placed into the full load shipper cases and the EPCDs will be affixed outside the accordingly shipper cases inside with IPCD.

3.6.无线探头 Data Loggers

3.6.1. 校验完的温湿度无线探头用于半周期确认。

Calibrated temperature and humidity data loggers were used in half cycle qualification runs.

3.6.2. 总计 6 个温度，3 个湿度探头依照验证方案附录 2 的要求放置在装载指定的位置。

A total of 6 T and 3 RH data loggers were placed in the locations stipulated in appendix 2 of the protocol.

3.7.结果 Results

3.7.1. 过程参数 Process Parameters

3.7.2. 半周期循环符合规定的过程参数，完成的循环参数报告（验证方案附录 1）和灭菌循环记录包括设定值及范围见本报告附录 3。

The three half cycle runs met the cycle parameters. The filled cycle parameter sheets (appendix 1 of the protocol) and the cycle run records including set points and tolerance are enclosed within this completion report in attachment 3.

3.8.装载的物理性质 Physical profiles of the loads

3.8.1. 装载的温湿度分布见附录 4

The temperature and humidity profiles are presented in attachment 4.

3.8.2. 装载的温湿度分布在半周期循环不同阶段的表现见如下列表：

A summary of the load response at different phases of the three half cycle runs is tabulated below:

表 1Table 1: 装载温度分布 Load Temperature Data Profile

PHASES 阶段	Load Parameter 装载参数	1st half cycle 半周期 1	Position 位置	2nd half cycle 半周期 2	Position 位置	3rd half cycle 半周期 3	Position 位置
Start of the cycle 循环开始	Min. Load Temp.最低装载温度	6.3℃	T1	5.0℃	T2	5.3℃	T2
Preconditioning 预热	Min. Load Temp.最低装载温度	6.3℃	T1	5.0℃	T2	5.3℃	T2
	Max. Load Temp.最高装载温度	43.1℃	T6	46.8℃	T5	41.8℃	T5
	Min. Load Humidity 最低湿度	73.7%	H3	44.5%	H2	51.6%	H3
	Max. Load Humidity 最高湿度	88.8%	H1	94.7%	H1	84.1%	H1
	Min. Load Temp. at the end of Preconditioning Phase 预热结束后的最低温度	29.8℃	T1	31.2℃	T1	30℃	T3
	Max. Load Temp. at the end of Preconditioning Phase 预热结束后的最高温度	43.1℃	T6	46.8℃	T5	41.8℃	T5
	Min. Load Humidity at the end of Preconditioning Phase 预热结束最低湿度	73.7%	H3	44.5%	H3	51.6%	H3
	Max. Load Humidity at the end of Preconditioning phase 预热结束最高湿度	88.1%	H1	80.8%	H1	67.0%	H2
EO Exposure time 灭菌暴露阶段	Min. Load Temp.最低装载温度	30.7℃	T3	31.8℃	T1	30.7℃	T3
	Max. Load Temp.最高装载温度	47.4℃	T6	49.6℃	T5	46.7℃	T5
	Average load Temp.平均装载温度	40.3℃	N/A	42.7℃	N/A	41.1℃	N/A
	Min. Load Humidity 最低装载湿度	71.1%	H2/H3	42.7%	H3	56.4%	H3
	Max. Load Humidity 最高装载湿度	90.1%	H1	85.8%	H1	69.1%	H2
Aeration 解析	Min. Temp.最低温度	35.9℃	T3	39.3℃	T1	36.2℃	T3
	Max. Temp.最高温度	47.4℃	T6	49.6℃	T5	46.7℃	T5

备注 Note: N/A-不存在

a. 完整的 PPQ 缺少一个正常的灭菌循环 Full PPQ missed one nominal full sterilization cycle.

b. 依据半周期循环确认的结果，进入灭菌柜的最低装载温度需大于≥ 5.0℃，灭菌循环开始装载的温度范围：

Minimum load temperature shall be ≥ 5.0℃ according to the half cycle qualification runs results.

观察项 Observations:

a.开始温度范围 The start-up point temperature was between the range of 5.0- 6.3°C.

b.预热结束后的温度范围 The end of preconditioning temperature was between the range of 29.8- 46.8°C.

c.预热结束后的湿度范围 The end of preconditioning RH was between the range of 44.5 - 88.1 %.

d.装载的冷点位置与表一相符 The cold spot in the loads were aligned with the locations identified in table 1.

3.8.3. 加药及清洗阶段的压力变化 Pressure rise during gas injection and washing phase

Table- 2 压力变化数据 Pressure rise profile

Phase 阶段	1st half cycle 半周期 1	2nd half cycle 半周期 2	3rd half cycle 半周期 3
EO pressure change (kpa) 加药后的压力变化	28.3	28.4	28.5
EO charge (min) 加药时间	11	7	12
Rate(kpa/min)速率	2.5	4.3	2.4
Final pressure (kpa) 最终压力	-38.0	-38.1	-38.4
Mass of EO used (kg) 使用的 EO 量	4	4	4
EO concentration (mg/L) EO 浓度	463.3	465.0	465.8

6.5 Method of determining EO gas concentration based on physical laws of perfect gas behavior

6.5.1 100 % EO sterilant

When the sterilant gas injected into the sterilizer chamber is 100 % EO, the mean EO gas density (concentration) within the chamber may be determined by using the relationship shown in Equation (5) and as shown in Example 1 as follows:

$$C_{eo} = \frac{M_{eo(g/mole)} P_{eo(atm)}}{R_{(liter-atm/Kelvin-mole)} T_{(Kelvin)}}, \qquad \text{(equation 5)}$$

where

M_{eo} = 44.054 g/mole (molecular weight of EO)
C_{eo} = mean EO gas concentration in mg/L
P_{eo} = partial pressure of EO gas injected into the chamber

Table- 2 清洗阶段压力变化数据 Pressure profile during washing/flushing phase

PHASES 阶段	1st half cycle 第一次半周期			2nd half cycle 第二次半周期			3rd half cycle 第三次半周期		
	抽真空时间 Time for vacuum (min)	压力变化 Pressure change (kpa)	速率 Rate (kpa/min)	抽真空时间 Time for vacuum (min)	压力变化 Pressure change (kpa)	速率 Rate (kpa/min)	抽真空时间 Time for vacuum (min)	压力变化 Pressure change (kpa)	速率 Rate (kpa/min)
The 1st vacuum 第一次抽真空	14	67.8	4.84	14	68	4.86	14	67.8	4.84
The 2nd vacuum 第二次抽真空	14	68.1	4.86	14	68	4.86	13	67.9	5.22
The 3rd vacuum 第三次抽真空	14	68.1	4.86	14	68.3	4.88	14	68	4.86
The fourth vacuum 第四次抽真空	14	68.1	4.86	13	68.3	5.25	14	68.2	4.87
The 5th vacuum 第 5 次抽真空	13	68.4	5.26	13	68.1	5.24	13	68.4	5.26
Air break 1 第一次进气	4	65.6	16.40	3	65.8	21.93	3	65.8	21.93
Air break 2 第二次进气	3	68	22.67	4	67.9	16.98	4	67.8	16.95
Air break 3 第三次进气	3	67.9	22.63	3	68.2	22.73	4	68	17.00
Air break 4 第四次进气	3	68.1	22.70	3	68.3	22.77	3	68	22.67
Air break5 第五次进气	3	68.3	22.77	4	68.1	17.03	3	68.3	22.77

对比此次半周期循环的气体注入阶段及清洗阶段压力的变化，真空度相似，再现性得以证实，由此可以证实物理性能（缺少一个完整的全周期循环）。

Comparing the pressure rise during gas injection and washing phase of this half cycle qualification runs, the vacuum rate are similar, reproducibility has been verified. Therefore the physical performance is qualified (missing one nominal full sterilization cycle).

3.9. 实施了生物指示剂培养（来自内置挑战装置,外置挑战装置）。

The biological indicators incubation (from IPCDs and EPCDs) was conducted .

3.9.1.1. 培养结果显示在三个半周期内所有生物指示剂（IPCD）均杀灭，EPCD 有部分 BI 存活。

The incubation results showed complete inactivation of the BIs from IPCD in three half cycle runs, partial BIs showed growth.

3.9.1.2. 阳性对照显示生长，阴性对照显示不生长。

All positives controls showed growth and all negative controls showed no growth.

3.9.1.3. 所有测试结果概述于表 4

Overall test results are summarized in the table # 4 below.

Table 4 - 生物指示剂无菌测试结果 BI Sterility Test Results

Cycle 循环	IPCD Results (No. of Positives / Total No. of BI Tested) 内置挑战装置 BI 阳性/总数	EPCD Results (No. of Positives / Total No. of BI Tested) 外置挑战装置 BI 阳性/总数
1st Half cycle	0/18	0/18
2nd Half cycle	0/18	0/18
3rd Half cycle	0/18	0/18

3.10. 结论 Conclusions

通过以上常规微生物测试，产品族的无菌保证水平 10^{-6} 得到确认，由此 MPQ 得到证实。

Through above routine microbiology testings, current product family SAL 10^{-6} is verified, so the MPQ is qualified.

3.11. 产品处置 Disposition of the products

此次半周期循环所采用的产品装载为模拟装载，故无需对产品进行处置。

The load used for this half cycle qualification is dunnage load, thereby no products disposal required.

4. 纠正措施 Corrective Actions:

在实施半周期循环确认过程中未发现偏差，故无需纠正措施。

There is no deviation reported during execution of this half cycle qualification runs, hence corrective action is not required.

5. 可交付性 Deliverables:

基于物理性能（PPQ，缺一正常全周期)和微生物性能（MPQ）的确认结果，现有灭菌柜已经通过确认，可用于硅胶引流产品族常规灭菌

Based on the results of physical performance (missing one nominal full cycle for PPQ) and microbiological performance qualification of half cycles qualification, existing sterilization chamber is qualified to run the sterilization cycle for current Silicone Drainage Product Family routine sterilization.

6. 附录 Appendices

Attachment 1 – 相关人员的培训记录 Training record of relevant staff

Attachment 2 – 仪表校验清单及验证记录 Instruments Calibration review check list and calibration records.

Attachment 3 - 灭菌循环记录（灭菌报告）Run records (half cycle run reports)

Attachment 4 – 装载温湿度分布数据 Load Temperature & humidity data and profiles.

Attachment 5 – 微生物确认测试报告（生物指示剂）Microbiological Qualification Test Reports (BI incubation results).

Attachment 6 – EO 气体及生物指示剂符合性证书 Certificates of compliance of EO gas and Biological indicator.