BIOTECH

Technical Report

USTR 3528

Kleenpak® HT Sterile Connector Validation Following New ½ in. Mold Tool and Component Introduction

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Contents

1 Validation Overview

1.1 Introduction

This report contains data applicable to Pall's Kleenpak HT sterile connectors that can be used to make sterile connections between tubing and other components in biopharmaceutical applications. Kleenpak HT sterile connectors allow for the dry connection of two separate fluid pathways, while maintaining the sterile integrity of both pathways. The connector consists of a male and female connector, each covered by a peel away strip that protects the port and maintains the sterility of the sterile fluid pathway.

Increased customer demand has driven the need to increase capacity of components used in the assembly of Kleenpak connectors, therefore new multi-cavity tooling has been created to increase the capacity. The new male spike plunger used on part number (p/n) KPCHT02M6 connectors, and the female dock used on p/n KPCHT02F6 connectors, are produced using two cavity tools (two connectors molded per cycle) to increase capacity over the existing single cavity tooling.

The purpose of this report is to document testing that has been performed to demonstrate the performance and suitability of the Kleenpak HT sterile connector following the introduction of the new tooling and components.

1.2 Summary of Conclusions

1.2.1 Extended Duration Testing

96 sterilized Kleenpak HT sterile connectors (half the connectors were gamma irradiated at 50 kGy ± 5 kGy and the other half were autoclaved at 130 °C for 75 minutes; 48 paired and actuated connectors) were subjected to continuous use at 3.0 barg, 40 °C for 30 days. All combinations of the new single piece male and female bodies from both cavity A and cavity B were connected and actuated with each other as well as with existing incumbent male and female bodies.

All Kleenpak HT sterile connectors passed the specified operating conditions for both sterilization methods.

Additional short-term testing was also performed on gamma irradiated Kleenpak HT sterile connectors. 96 connectors (48 paired and actuated connectors) were split between two tests. The first test was undertaken at 1.5 barg, 2 °C – 8 °C for 24hours. The second test was undertaken for 8 hours at 4.0 barg, 21 °C (ambient). All combinations of the new male and female bodies from both cavity A and cavity B were connected and actuated with each other as well as with existing incumbent male and female bodies.

All Kleenpak HT sterile connectors passed the two short term specified operating conditions when gamma irradiated.

1.2.2 Extractables Testing

Total organic carbon (TOC) testing and inductively coupled plasma mass spectrometry (ICP/MS) were performed on the incumbent and new single piece components (p/n KPCHT02M6 and KPCHT02F6) as the elemental composition of the injection mold tooling and molding parameters are different. There is no change to the polymeric materials of construction.

Comparative TOC values indicated no meaningful differences between the incumbent and post change substrate. This serves to verify that any differences in molding parameters are negligible with respect to impact on the material.

1.2.3 Probe Insertion Testing

Probe insertion testing was performed on new connectors to confirm sensor probes typically inserted through these connectors can pass freely through the inside diameter of the connector without obstruction or difficulty.

All probe sensors passed freely through the bore of the new Kleenpak HT sterile connectors with the same ease as the incumbent connectors.

1.2.4 Mold Tool Validation

The new Kleenpak HT sterile connector components (male spike plunger and female dock components) molding process was validated to confirm that the components could be injection molded to drawing specification in a repeatable and robust way.

1.2.5 Assembly Process Validation

The new Kleenpak HT sterile connector components were assessed to confirm that they could be fully assembled into finished goods utilizing the current production process settings, including all necessary in process and release testing requirements.

2 Extended Duration Testing

2.1 Introduction

The purpose of these tests was to demonstrate that the new Kleenpak HT sterile connectors can withstand the specified extended duration usage conditions of continuous 30-day use at 3.0 barg, 40 °C under specified sterilization parameters. In addition, short term testing for 24 hours at 1.5 barg, 2 °C – 8 °C and 8 hours at 4.0 barg, 21 °C for gamma irradiated connectors was also performed.

2.2 Summary of Methods

Testing was performed on connectors assembled and actuated using the assembly aid (p/n KPC01A) and subjected to appropriate pre-sterilization treatment (connectors were gamma irradiated at a dose of 50 kGy ± 5 kGy or autoclaved for 75 minutes at 130 °C). The actuated connectors were connected to a test rig consisting of a pump and controller, water bath, pressure gauge and regulator, and size appropriate braid reinforced tubing and manifolds. Each test was primed to remove air bubbles, set at the correct temperature and the pressure increased to the specified parameter.

2.3 Results

All Kleenpak HT sterile connectors passed the requirements for the extended duration testing at the specified sterilization conditions.

Table 1

Extended duration testing results

Test Description	Number of Connector Samples	Sterilization Conditions	Test Outcome
30 days, 3.0 bag, 40 °C	48	Autoclaved	Pass
30 days, 3.0 barg, 40 °C	48	Gamma irradiated	Pass
24 hours, 1.5 barg, 2 °C – 8 °C	48	Gamma irradiated	Pass
8 hours, 4.0 barg, 21 °C	48	Gamma irradiated	Pass

2.4 Conclusion

A total of 192 connectors (96 paired connectors) were tested, 48 connectors (24 paired connectors) per test. All Kleenpak HT sterile connectors passed the requirement of no leaks during the test period at the specified test and sterilization parameters.

3 Extractables Testing

3.1 Introduction

The purpose of these tests was to compare the TOC and elemental impurities profiles of the incumbent and new multi-cavity injection mold tooling that produces the male spike plunger and female dock components.

3.2 Summary of Methods

Three pairs of (male and female) connectors (½ in. p/n KPCHT02M6 / KPCHT02F6) were immersed in 300 mL of water in a clean 500 mL amber glass container with a polytetrafluoroethylene (PTFE) cap. The samples were extracted with agitation at 40 °C for seven days. The negative control was generated by incubating 300 mL of water in the same glass container under the same conditions as the samples. All samples were analyzed by TOC and ICP/MS.

3.3 Results

Table 2

Total organic carbon results for incumbent and post-change connectors

	Incumbent Connectors		Post-Change Connectors	
	Lot Number 109801F / 10980M	Lot Number 109801F / 10980M	Lot Number T-0970	Lot Number T-0970
Method	**7 Days**	**7 Days**	**7 Days**	**7 Days**
TOC (µg/mL)	0.252	0.242	0.295	0.274
Average TOC (µg/mL)	0.247		0.284	
Post change (%) variation	0		15.2	

Table 3

Elemental impurity results for incumbent and post-change connectors

					Incumbent Connectors		Post-Change Connectors	
Element		**ICH Q3D Class**	**Limit of detection – (LOD) (ng/mL)**	**Limit of quantitation – (LOQ) (ng/mL)**	**Lot Number 109801F / 10980M**	**Lot Number 109801F / 10980M**	**Lot Number T-0970**	**Lot Number T-0970**
Cadmium	Cd	1	0.020	0.065	-	-	-	-
Lead	Pb	1	0.070	0.235	-	-	-	-
Arsenic	As	1	0.331	1.102	-	-	-	-
Mercury	Hg	1	1.032	3.439	-	-	-	-
Cobalt	Co	2A	0.054	0.179	-	-	-	-
Vanadium	V	2A	1.653	5.511	-	-	-	-
Nickel	Ni	2A	0.301	1.003	-	-	-	-
Thallium	Ti	2B	0.085	0.282	-	-	-	-
Gold	Au	2B	3.679	12.265	-	-	-	-
Palladium	Pd	2B	0.029	0.098	-	-	-	-
Iridium	Ir	2B	0.031	0.103	-	-	-	-
Osmium	Os	2B	1.355	4.516	-	-	-	-
Rhodium	Rh	2B	0.005	0.018	-	-	-	-
Ruthenium	Ru	2B	0.014	0.046	-	-	-	-
Selenium	Se	2B	2.601	8.669	-	-	-	-
Silver	Ag	2B	0.011	0.036	-	-	-	-
Platinum	Pt	2B	0.083	0.276	-	-	-	-
Lithium	Li	3	0.753	2.511	-	-	-	-

Antimony	Sb	3	1.175	3.916	-	-	-	-
Barium	Ba	3	0.173	0.577	-	-	-	-
Molybdenum	Mo	3	0.532	1.775	-	-	-	-
Copper	Cu	3	0.195	0.650	-	-	-	-
Tin	Sn	3	0.586	1.952	-	-	-	-
Chromium	Cr	3	0.509	1.698	-	-	-	-

3.4 Conclusion

The results of the TOC testing showed an average increase of 37.5 ppb TOC values (about 15% difference) between the incumbent and new materials. As this value is within typical TOC measurement variation and uncertainty (typically within 20%), test results indicate no meaningful differences between the incumbent and new samples.

4 Probe Insertion Testing

4.1 Introduction

The purpose of these tests is to confirm that sensor probes, typically inserted through the male connector p/n KPCHT02M6, can pass freely along the inside diameter of the new p/n KPCHT02M6 spike plunger.

4.2 Summary of Methods

Six probes from three different manufacturers were inserted into a total of twelve male spike plungers, four from the incumbent single cavity tooling and four each from both cavity A and B from the new tooling.

4.3 Results

Table 4

Probe insertion testing results

Sensor Probe	Incumbent				Cavity A				Cavity B			
	1	2	3	4	1	2	3	4	1	2	3	4
Broadley James® SN00423 (stainless steel)	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
Broadley James SN160 (stainless steel)	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
Mettler Toledo® P52200966 (stainless steel)	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
MT 104054481 (pH) (glass)	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
MT P52206120 (stainless steel)	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
Hamilton® DO SU ARC120C (stainless steel)	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass

4.4 Conclusion

The new male spike plungers produced from the new tooling (cavity A and cavity B) are suitable for applications requiring sensor probe insertion through a KPCHT02M6 connector.

5 Mold Tool Validation

5.1 Introduction

The purpose of validation is to confirm the new Kleenpak HT sterile connector components' (male spike plunger and female dock components) molding process can produce parts to specification repeatably and robustly meeting all in process and release quality inspection criteria.

5.2 Summary of Methods

The new mold tooling was subject to an installation, operational and performance qualification (IQ/OQ/PQ) validation process at the supplier. The IQ stage confirmed function of the new tooling and that it was built according to specification. The OQ stage defined the process settings (temperature, pressure and time) to produce components to the correct dimensional specifications. The PQ stage confirmed the repeatability and robustness of the molding process.

Ultimately, three PQ runs of 3000 components for both the male spike plunger and female dock were completed. 9000 components per tool, 18000 components molded in total. Each PQ run had 30 shots (two components per shot – 60 components in total) randomly taken across each run for dimensional measurement of the critical to quality (CTQ) dimensions to confirm they are to specification. An additional 30 shots per run was also taken for visual and cosmetic inspection.

5.3 Results

The output from the PQ report was that all components measured and inspected met the specification set at OQ and all CTQ dimensions were to specification.

5.4 Conclusion

The mold tool and process was ready for full scale production following approval.

6 Assembly Process Validation

6.1 Introduction

The new Kleenpak HT sterile connector components were assessed to confirm that they could be fully assembled into finished goods utilizing the current production process settings, including all necessary in process and release testing requirements.

6.2 Summary of Methods

There are four production lines assembling the Kleenpak HT sterile connectors. Each line was assessed as detailed below.

Table 5

Engineering study for Kleenpak HT sterile connectors

Production Line	Product Produced	Test Quantity
Female line	KPCHT02F6 (female)	150
Male line	KPCHT02M6 (male)	150
Combi line	KPCHT02F6 (female)	150
Combi line	KPCHT02M6 (male)	150
Line 4	KPCHT02F6 (female)	150
Line 4	KPCHT02M6 (male)	150

Testing for each run is detailed below in Table 6.

Table 6

Test details

Test Description	Sampling Method	Sampling Quantity
Seal integrity	5 samples every 30 minutes	125
Visual / membrane peel	5 samples every 30 minutes	125
Cleanliness (test for particulate cleanliness with counts determined microscopically)	1.0% per lot (3 samples per lot of 2400)	13
Pyrogenicity - Limulus Amebocyte Lysate (LAL) (USP <85>)	3 samples per day lot	5

6.3 Results

Table 7

Peel and seal integrity results for Kleenpak HT sterile connectors

Production Line	Product Produced	Peel Result	Seal Integrity
Female line	KPCHT02F6 (female)	Pass	Pass
Combi line	KPCHT02F6 (female)	Pass	Pass
Line 4	KPCHT02F6 (female)	Pass	Pass

Table 8

O-ring, leak test, visual damage, and assembly results for Kleenpak HT sterile connectors

Production Line	Product Produced	O-Ring Seated	Leak Test	Visual Damage	Assembly
Male line	KPCHT02M6 (male)	Pass	Pass	Pass	Pass
Combi line	KPCHT02M6 (male)	Pass	Pass	Pass	Pass
Line 4	KPCHT02M6 (male)	Pass	Pass	Pass	Pass

Table 9

Cleanliness and LAL (USP <85>) results for Kleenpak HT sterile connectors

Production Line	Particulate	LAL
Female line	Pass	Pass
Male line	Pass	Pass
Combi line	Pass	Pass
Combi line	Pass	Pass
Line 4	Pass	Pass
Line 4	Pass	Pass

6.4 Conclusion

The new components meet all the testing and assembly requirements of all the production lines.

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