DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center - WO66-G609
Silver Spring, MD 20993-0002

October 30, 2015

ZOLL Circulation, Inc.
Mr. Sam Nanavati
V.P., Quality Assurance and Regulatory Affairs
2000 Ringwood Avenue
San Jose, California 95131

Re: K150046
Trade/Device Name: Cool Line Intravascular Heat Exchange Catheter, ICY Intravascular Heat Exchange Catheter, Quattro Intravascular Heat Exchange Catheter, Start-Up Kit (SUK)
Regulation Number: 21 CFR 870.5900
Regulation Name: Thermal Regulating System
Regulatory Class: Class II
Product Code: NCX
Dated: September 30, 2015
Received: October 2, 2015

Dear Mr. Sam Nanavati:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act and the limitations described below. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you; however, that device labeling must be truthful and not misleading.

The Office of Device Evaluation has determined that there is a reasonable likelihood that the Cool Line Intravascular Heat Exchange Catheter will be used for an intended use not identified in the proposed labeling and that such use could cause harm. Therefore, in accordance with Section 513(i)(1)(E) of the Act, the following limitation must appear in the Warnings section of the device's labeling as a box warning immediately following the indications for use statement:

> The safety of this device has not been demonstrated for fever reduction in patients presenting with subarachnoid hemorrhage or primary traumatic brain injury. The safety and effectiveness of this device was examined in a randomized controlled trial of 296 patients. The mortality results reported in this trial, for the four patient cohorts enrolled,

are presented in the table below (CI – cerebral infarction, ICH – intracerebral hemorrhage, PTBI – primary traumatic brain injury, SAH – subarachnoid hemorrhage).

Mortality by Diagnosis (ITT analysis)

	Cool Line			Control			
	n	N	%	n	N	%	p*
CI	3	16	18.8	3	14	21.4	0.74
ICH	8	33	24.2	7	27	25.9	1.00
PTBI	10	44	22.7	4	38	10.5	0.24
SAH	13	61	21.3	7	63	11.1	0.15

*Fischer's exact test

For more details on the clinical trial results please refer to Physician's Manual – "Normothermia for the Neuro-critically Ill stroke patient" PN 8700-0634-01.

Please note that the above labeling limitation is required by Section 513(i)(1)(E) of the Act. Therefore, a new 510(k) is required before these limitations are modified in any way or removed from the device's labeling. This limitation does not apply to the ICY and Quattro Intravascular Heat Exchange Catheters.

The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and permits your device to proceed to the market. This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification if the limitation statement described above is added to your labeling.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part

807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Jonette R. Foy -S

William H. Maisel, MD, MPH
Director (Acting)
Office of Device Evaluation
Deputy Center Director for Science
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K150046

Device Name
Cool Line Intravascular Heat Exchange Catheter, ICY Intravascular Heat Exchange Catheter, Quattro Intravascular Heat Exchange Catheter, Start-Up Kit (SUK)

Indications for Use *(Describe)*
The Cool Line Catheter Model CL-2295A when used with the ZOLL Thermal Regulation System is indicated for use in fever reduction, as an adjunct to antipyretic therapy, in adult patients with cerebral infarction and intracerebral hemorrhage who require access to the central venous circulation and who are intubated and sedated.

WARNING – Fever Reduction

The safety of this device has not been demonstrated for fever reduction in patients presenting with subarachnoid hemorrhage or primary traumatic brain injury. The safety and effectiveness of this device was examined in a randomized controlled trial of 296 patients. The mortality results reported in this trial, for the four patient cohorts enrolled, are presented in the table below (CI – cerebral infarction, ICH – intracerebral hemorrhage, PTBI – primary traumatic brain injury, SAH – subarachnoid hemorrhage).

Mortality by Diagnosis (ITT analysis)

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SAH	13	61	21.3	7	63	11.1	0.15

*Fischer's exact test

For more details on the clinical trial results please refer to Physician's Manual – "Normothermia for the Neuro-critically Ill stroke patient" PN 8700-0634-01.

The ZOLL ICY Intravascular Heat Exchange Catheter Model IC-3893-A, connected to the ZOLL CoolGard 3000/ Thermogard XP Thermal Regulation System, is indicated for use:

- In cardiac surgery adult patients to achieve and/or maintain normothermia during surgery and recovery/intensive care, and
- To induce, maintain and reverse mild hypothermia in neurosurgery adult patients in surgery and recovery/intensive care.

The ZOLL Quattro Catheter Model IC-4593, connected to a ZOLL Thermal Regulation System, is indicated for use:

- In cardiac surgery adult patients to achieve and/or maintain normothermia during surgery and recovery/intensive care, and
- To induce, maintain and reverse mild hypothermia in neurosurgery adult patients in surgery and recovery/intensive care.

The Start-Up Kit (SUK) is intended to control patient core temperature using heat exchange fluid in conjunction with CoolGard 3000 or Thermogard XP system and ZOLL Heat Exchange Catheters, but does not have a specific independent indications for use.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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PREMARKET NOTIFICATION 510(K) SUMMARY

Date Prepared:	September 25, 2015
Submitter:	ZOLL Circulation, Inc.
Address:	2000 Ringwood Avenue San Jose, CA 95131
Phone:	408-419-2950
Fax:	408-541-1030
Contact Person:	Sam Nanavati, VP, Quality and Regulatory Affairs
Trade Name/Proprietary Name:	Cool Line® Intravascular Heat Exchange Catheter ICY® Intravascular Heat Exchange Catheter Quattro™ Intravascular Heat Exchange Catheter Start-Up Kit (SUK)
Common Name:	Central Venous Catheter (short term) and Thermal Regulating System
Classification/Name:	Class II; System, Hypothermia, Intravenous, Cooling
Regulation:	21 CFR 870.5900, Thermal Regulating System
Product Code:	NCX
Legally marketed devices to which substantial equivalence is claimed:	Cool Line Catheter Kit Model CL-2295A (K101987); ICY Catheter Kit Model IC-3893A (K101987); Quattro Catheter Kit Model IC-4593 (K101987); Start-Up Kit Model CG-500D and Model CG-500D EX (K014241)

I. Device Description

The ZOLL Intravascular Heat Exchange Catheters (Cool Line, ICY, and Quattro - ZOLL Catheters) are sterile, single use heparin coated flexible catheters designed for placement in the femoral, jugular, or subclavian veins. The Cool Line Catheter contains two heat exchange balloons, the ICY Catheter contains three heat exchange balloons, and the Quattro Catheter contains four heat exchange balloons.

The ZOLL Catheters are connected to a single use, disposable Start-Up Kit (SUK) and the CoolGard 3000® or Thermogard XP® Console. The catheters connect to the console coolant well via tubing integral to the SUK. The catheter is connected to the SUK by connecting the male outflow Luer of the SUK to the female inflow Luer of the catheter and the female inflow Luer of the SUK to the male outflow Luer of the catheter. Both SUK Luers, in turn, are connected via tubing to a heat exchange coil through which saline circulates. The coil is placed in a coolant well located in the console. The controlled temperature saline is circulated through the closed-loop circuit of the SUK and catheter using the console pump, after which the saline is then returned within the SUK to the console heater and chiller coolant well via the catheter's outflow lumen.

The Catheters, SUK and the CoolGard 3000 or Thermogard XP Console are supplied separately. The ZOLL Intravascular Heat Exchange System is also designed for use with an off-the-shelf temperature probe, which is supplied separately and not manufactured by ZOLL.

II. Indications for Use

The intended use / indications for use of the modified Cool Line, ICY, and Quattro Catheters are identical to the intended use / indications for use of the predicate Cool Line, ICY, and Quattro Catheters [cleared by FDA on October 12, 2010 under 510(k) K101987], which is as follows:

Cool Line Intravascular Heat Exchange Catheter

The Cool Line Catheter Model CL-2295A when used with the ZOLL Thermal Regulation System is indicated for use in fever reduction, as an adjunct to antipyretic therapy, in adult patients with cerebral infarction and intracerebral hemorrhage who require access to the central venous circulation and who are intubated and sedated.

Warning – Fever Reduction

The safety of this device has not been demonstrated for fever reduction in patients presenting with subarachnoid hemorrhage or primary traumatic brain injury. The safety and effectiveness of this device was examined in a randomized controlled trial of 296 patients. The mortality results reported in this trial, for the four patient cohorts enrolled, are presented in the table below (CI – cerebral infarction, ICH – intracerebral hemorrhage, PTBI – primary traumatic brain injury, SAH – subarachnoid hemorrhage).

Mortality by Diagnosis (ITT analysis)

	Cool Line			Control			
	n	N	%	n	N	%	p*
CI	3	16	18.8	3	14	21.4	0.74
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PTBI	10	44	22.7	4	38	10.5	0.24
SAH	13	61	21.3	7	63	11.1	0.15

*Fischer's exact test

For more details on the clinical trial results please refer to Physician's Manual – "Normothermia for the Neuro-critically Ill stroke patient" PN 8700-0634-01.

ICY Intravascular Heat Exchange Catheter

The ZOLL ICY Intravascular Heat Exchange Catheter Model IC-3893-A, connected to the ZOLL CoolGard 3000/Thermogard XP Thermal Regulation System, is indicated for use:

- In cardiac surgery adult patients to achieve and/or maintain normothermia during surgery and recovery/intensive care, and
- To induce, maintain and reverse mild hypothermia in neurosurgery adult patients in surgery and recovery/intensive care.

Quattro Intravascular Heat Exchange Catheter

The ZOLL Quattro Catheter Model IC-4593, connected to a ZOLL Thermal Regulation System, is indicated for use:

- In cardiac surgery adult patients to achieve and/or maintain normothermia during surgery and recovery/intensive care, and
- To induce, maintain and reverse mild hypothermia in neurosurgery adult patients in surgery and recovery/intensive care.

The SUK is intended to control patient core temperature using heat exchange fluid in conjunction with CoolGard 3000 or Thermogard XP system and ZOLL Heat Exchange Catheters, but does not have a specific independent indications for use.

III. Technological Characteristics of the Device Compared to the Predicate Device

The modified SUK and the modified Cool Line, ICY, and Quattro Intravascular Heat Exchange Catheters are substantially equivalent to the 510(k) cleared Cool line, ICY and Quattro Catheters (SUK: K072234; Catheters: K101987), with regard to intended use / indications for use, technological characteristics, and principles of operation. **Table 1** and **Table 2** provide a comparison of the similarities and differences in technological characteristics between the modified SUK and Cool Line, ICY, and Quattro Catheters, to the cleared SUK and Cool Line, ICY, and Quattro Catheters.

Table 1. Comparison of Proposed Modified Catheters with Predicates

Characteristic	**PREDICATE DEVICES ZOLL Cool Line, ICY and Quattro Catheters with ZOLL Standard Luers**	**SUBJECT DEVICES ZOLL Cool Line, ICY and Quattro Catheters with ZOLL Custom Luers (modified)**
510(k) Number	K101987	K150046
Class	II	Same
Classification/ Regulation Name	System, Hypothermia, Intravenous, Cooling/Thermal Regulating System	Same
Regulation Number	21 CFR 870.5900	Same
Product Code	NCX	Same
Insertion Site	Cool Line – femoral vein, jugular vein, subclavian vein ICY – femoral vein Quattro – femoral vein	Same
Heparin Coating	SurModics Applause Heparin Coating	Same
Luer Designs	Inflow and Outflow Luers: ZOLL Standard Luers Infusion Luers: ZOLL Standard Luers Vent Caps: ZOLL Standard Vent Caps	Inflow and Outflow Luers: ZOLL Custom Luers Infusion Luers: ZOLL Standard Luers Vent Caps: ZOLL Custom Vent Caps
Luer Materials	Base material is polyurethane (for all luers except for vent caps) Inflow and outflow Luers: Polyurethane: Tecoplast OP-770-321 Teal Green Distal infusion Luer: Polyurethane: Tecoplast OP-770-477 Brown Medial infusion Luer: Polyurethane: Tecoplast	Same Inflow and outflow Luers: Polyurethane: Tecoplast OP-770-164 Orange Distal infusion Luer: Same as predicate (except pad printing has changed from black ink to white ink) Medial infusion Luer: Same as predicate

Characteristic	PREDICATE DEVICES ZOLL Cool Line, ICY and Quattro Catheters with ZOLL Standard Luers	SUBJECT DEVICES ZOLL Cool Line, ICY and Quattro Catheters with ZOLL Custom Luers (modified)
	OP-770-White Proximal infusion Luer: Polyurethane: Tecoplast OP-770-541 Dark Blue Male vent cap: ABS: (purchased component) Merit Medical (P/N 101031001) Female vent cap: Polypropylene: (purchased component) Merit Medical (P/N 101030002)	 Proximal infusion Luer: Same as predicate (except pad printing has changed from black ink to white ink) Male vent cap: ABS: Ineos Lustran (P/N 348-012002) Female vent cap: ABS: Ineos Lustran (P/N 348-012002)
Catheter working length (tip to manifold)	Cool Line – 22 cm ICY – 38 cm Quattro – 45 cm	Same
Shaft diameter	9.3 Fr	Same
Number of lumens	5 lumens: 2 infusion, 1 guidewire (plus infusion), 1 inflow, 1 outflow	Same
Guidewire Compatibility	0.032”	Same
Heat Exchange Balloons	Cool Line – 2 (straight/ coaxial) ICY – 3 (straight/coaxial) Quattro – 4 (straight/coaxial)	Same
Flow Rate (by lumen)	Cool Line Distal - 2100 mL/hr Medial - 1200 mL/hr Proximal - 1400 mL/hr ICY Distal – 1700 mL/hr Medial – 900 mL/hr Proximal – 1200 mL/hr Quattro Distal – 1300 mL/hr Medial – 800 mL/hr Proximal – 1100 mL/hr	Same
Approx. Inflated Balloon OD (Cross-sectional Area)	Cool Line: ~5mm ($20mm^2$) ICY and Quattro: ~8mm ($50mm^2$)	Same
Heat Exchange Power	Cool Line – 65 Watts nominal ICY – 140 Watts nominal Quattro – 190 Watts nominal	Same

Characteristic	PREDICATE DEVICES ZOLL Cool Line, ICY and Quattro Catheters with ZOLL Standard Luers	SUBJECT DEVICES ZOLL Cool Line, ICY and Quattro Catheters with ZOLL Custom Luers (modified)
Materials: Shaft Balloon	Polyurethane PET and Polyurethane (ICY and Quattro) Polyurethane (Cool Line)	Same
Sterilization	Ethylene Oxide (EO)	Same

** The Indication for Use for the Cool Line Catheter also includes the following black box warning:

Warning – Fever Reduction
The safety of this device has not been demonstrated for fever reduction in patients presenting with subarachnoid hemorrhage or primary traumatic brain injury. The safety and effectiveness of this device was examined in a randomized controlled trial of 296 patients. The mortality results reported in this trial, for the four patient cohorts enrolled, are presented in the table below (CI – cerebral infarction, ICH – intracerebral hemorrhage, PTBI – primary traumatic brain injury, SAH – subarachnoid hemorrhage).

Mortality by Diagnosis (ITT analysis)

	Cool Line			Control			
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SAH	13	61	21.3	7	63	11.1	0.15

*Fischer's exact test

For more details on the clinical trial results please refer to Physician's Manual – "Normothermia for the Neuro-critically Ill stroke patient" PN 8700-0634-01.

Table 2. Comparison of Proposed Modified Start-Up Kit with Predicates

Characteristic	PREDICATE DEVICES ZOLL Start-Up Kit with ZOLL Standard Luers	SUBJECT DEVICES ZOLL Start-Up Kit with ZOLL Custom Luers (modified)
510(k) Number	K014241	K150046
Intended Use	To control patient core temperature using heat exchange fluid in conjunction with CoolGard 3000 or Thermogard XP system and ZOLL Heat Exchange Catheters	Same
Indications for Use	Start-Up Kit does not have a specific independent indications for use	Same
Class	II	Same
Classification/ Regulation Name	System, Hypothermia, Intravenous, Cooling/Thermal Regulating System	Same
Regulation Number	21 CFR 870.5900	Same
Product Code	NCX	Same
Patient Contact	Indirect patient contact	Same
Luer Function	Join the SUK to the InFlow/OutFlow Lumens of the catheters, and allow saline to circulate through the catheter/SUK fluid path	Same

Characteristic	PREDICATE DEVICES ZOLL Start-Up Kit with ZOLL Standard Luers	SUBJECT DEVICES ZOLL Start-Up Kit with ZOLL Custom Luers (modified)
Supplied 20 ml Sterile Deflation (Slip-Fit) Syringe	Syringe not provided with SUK	Syringe, compatible with new custom Luer locks, provided with SUK for optional removal of saline from catheter heat exchange balloons prior to catheter removal
Luer Materials: SUK Female Luer (InFlow) SUK Male Luer (OutFlow)	 PVC: Alpha Gary 2212-RHT/1-118 Clear Acrylic: 65117	 PVC:Alpha Gary 2212-RHT/1-118 UN2243 Orange PVC:Alpha Gary 2212-RHT/1-118 UN2243 Orange
Sterilization	Provided sterile (Gamma sterilization)	Same

IV. Summary of the Nonclinical Tests Performed

Nonclinical testing was performed to ensure that the modified SUK and the modified Cool Line, ICY, and Quattro Intravascular Heat Exchange Catheters meet their predetermined design and performance specifications and that the product is substantially equivalent to the predicate devices (SUK: K014241; Catheters: K101987).

The modified SUK and the modified Cool Line, ICY, and Quattro Intravascular Heat Exchange Catheters are identical to the 510(k) cleared SUK and 510(k) cleared Cool Line, ICY, and Quattro Intravascular Heat Exchange Catheters in terms of intended use/indications for use and principles of operation, and the modified devices have equivalent technological characteristics to the cleared devices. Nonclinical testing completed includes Packaging validation (SUK only), Bench Performance, Biocompatibility, and Usability Testing. The non-clinical test results demonstrate that the modified devices continue to meet product design specifications.

Bench Performance

Packaging Validation

Packaging performance testing of the modified SUK was performed to verify that following exposure to simulated shipping conditions, the addition of the sterile packaged 20 mL Deflation (Slip-Fit) syringe to the outside of the sterilized SUK packaging does not impact the integrity of the SUK sterile packaging. Packaging testing completed is shown in **Table 3**.

Table 3. Start-Up Kit Packaging Testing

Test Name	Test Method Summary	Results
Visual Inspection	Visual inspection to inspect shipping boxes and trays for damage.	All shipping boxes and trays were undamaged.
SUK Package Seal Visual Integrity	Visual inspection to inspect the package seal in the area where the syringe bag is attached.	All package seals and tray seals were undamaged.
Syringe Pouch Seal Visual Integrity & Adhesion to Tyvek	Visual inspection of the affected area to inspect the package seal area	All syringe pouch seals and the film and Tyvek portion of the pouches were undamaged.

Test Name	Test Method Summary	Results
	of the syringe bag and film and Tyvek portion of the pouch.	
SUK Package Seal Peel Test	Peel testing of the affected area to ensure that seal peel data is not less than specified acceptance criteria	All SUK package seals were undamaged.

In addition, testing was performed (following exposure to simulated shipping conditions and packaging testing) to verify that product design specifications were met at T=0. Bench performance testing completed is shown in **Table 4**.

Table 4. Start-Up Kit Performance Testing

Test Name	Test Method Summary	Results
SUK Flow Test	To verify that air flows through the SUK system.	Air flowed through all SUK systems.
SUK High Pressure Leak Test	To verify no leaks below specified acceptance criteria.	No leaks were noted below the specified pressure.
Modified SUK Indwell Life Test	To verify that Custom Luers and SUK Tubing are able to function normally at specified temperatures for the labeled indwell period.	All custom Luers and SUK tubing were able to function normally for 7 days at the specified temperature.
SUK Tubing to Luer Tensile	To verify that SUK Tubing and Custom Luers conform to EN ISO 10555-1:2013 and minimum specified acceptance criteria.	The tensile strength of all inflow and outflow tubes to Luers met the requirements of ISO 10555-1:2013.

Bench Performance

Bench Performance Testing was conducted on samples of the Cool Line Intravascular Heat Exchange Catheter (as a representative model for all three catheters subject to the same modifications) to verify that product design specifications were met at T=0. The Luers and Extension tubings are identical in all models. Testing completed is shown in **Table 5**.

Table 5. Catheter Performance Testing

Test Name	Test Method Summary	Results
Visual Inspection	Visual inspection to inspect for Luers, caps, and extension tubes for correct colors.	All Luer colors met the requirements of associated drawings.
Dimensional Measurement of Extension Tube Lengths	Verify dimensions of extension tube lengths.	All extension tubes met specific dimensional specifications.
Guidewire Passage	Verify ability to frontload, backload, and remove J-tip 0.032" guidewire from catheter.	The J-tip 0.032" guidewire was able to be frontloaded, backloaded, and removed from all catheters.
Ink Stability	Verify that pad printed ink does not smudge or come off when tested in accordance with specified acceptance criteria.	The pad printed ink on all infusion Luers remained legible after rubbing with alcohol.
Alcohol Resistance	Verify that Luers do not craze or crack when tested in accordance with specified acceptance criteria.	No Luers showed evidence of crazing or cracking after being soaked in alcohol.

Test Name	Test Method Summary	Results
Balloon Deflation Using Deflation Syringe (20 mL Slip-Fit)	Verify that catheter balloons collapse upon aspiration at specified temperature using supplied slip-fit syringe.	All catheter balloons collapsed upon aspiration using the supplied slip fit syringe.
Balloons Leakage Upon Aspiration Using the Supplied Deflation (20 mL Slip-Fit) Syringe	To verify that catheter balloons conform to EN ISO 10555-1:2013 (must not show air leakage during aspiration).	No air leakage was noted from the catheter balloons during aspiration using the supplied slip fit syringe.
Heat Exchange Power	To verify that the modified catheters meet specified acceptance criteria.	All catheters met the heat transfer performance requirement.
Ultimate Burst/Leak (All Luers) - Embolic Failure	To verify that catheter Luers conform to EN ISO 10555-1:2013 (must meet minimum static pressure at specified temperature without embolic failure).	All catheters were able to withstand 100-110 psi static pressure at 37ºC without embolic failure.
Catheter Inflow/Outflow Custom Luers connected to SUK Inflow/Outflow Pressure Test	To verify that catheter inflow/outflow Luers and extensions withstand minimum static pressure for specified period of time.	All Luers and extension tubes were able to withstand a minimum static pressure while connected to an SUK for a specified period of time.
Modified Catheter Indwell Life	To verify that catheter Luers and extensions are able to function normally for the labeled indwell period.	All Luers and extension tubes were able to function normally for seven days.
Extension Tubing to Luer Tensile.	To verify that extensiuon tubing to Luer joints conform to EN ISO 10555-1:2013 (must meet minimum strength).	All catheter joints demonstrated minimum tensile strength in accordance with the requirements of EN ISO 10555-1:2013.

Where applicable, testing was performed in accordance with the following standards:

- ISO 10555-1:2013 - Sterile, single-use intravascular catheters Part 1. General requirements

The results of design verification testing performed demonstrate that the modified SUK and the modified Cool Line, ICY, and Quattro Intravascular Heat Exchange Catheters meet their design performance specifications at T=0.

Additional testing was conducted as part of Testing to Luer Standards on the injection molded components used to manufacture the modified SUK and the modified Cool Line, ICY, and Quattro Intravascular Heat Exchange Catheters. Results of testing verify compliance to the following applicable standard:

- ISO 594-1:1986 - Conical fittings with a 6% (Luer) taper for syringes, needles and certain other medical equipment Part 1: General requirements

In addition, tests methods similar to those specified in the following standard were used to test the Custom Luers with Custom reference fittings:

- ISO 594-2:1998 – Conical fittings with a 6% (Luer) taper for syringes, needles and certain other medical equipment Part 2: Lock fittings

Testing completed is shown in **Table 6**.

Table 6. Luer Performance Testing

Test Name	Test Method Summary	Results
Critical Dimensions Inspection	Critical dimensions must meet the dimensional tolerances for the Critical dimensions, of the respective drawing	All samples met the dimensional tolerances for the critical dimensions.
Gauging	Tested using test method similar to test specified in ISO594-1&2 (§4.1)	All samples met the requirements of the test method used.
Water/Liquid Leakage	Tested using test method similar to test specified in ISO594-1&2 (§4.2.1)	All samples met the requirements of the test method used.
Air Leakage	Tested using test method similar to test specified in ISO594-2 (§4.2.2)	All samples met the requirements of the test method used.
Separation Force	Tested using test method similar to that specified in ISO594-2 (§4.3)	All samples met the requirements of the test method used.
Unscrewing Torque	Tested using test method similar to that specified in ISO594-2 (§4.4)	All samples met the requirements of the test method used.
Ease of Assembly	Tested using test method similar to that specified in ISO594-2 (§4.5 b)	All samples met the requirements of the test method used.
Resistance to Overriding	Tested using test method similar to that specified in ISO594-2 (§4.6)	All samples met the requirements of the test method used.
Stress Cracking	Tested using test method similar to that specified in ISO594-2 (§4.7)	All samples met the requirements of the test method used.

Based on the test results obtained, it can be concluded that all of the standard and custom catheter Luers, custom SUK Luers, and custom catheter vented caps are qualified for use in the assemblies used to manufacture the modified SUK and the modified Cool Line, ICY and Quattro Intravascular Heat Exchange Catheters.

Biocompatibility

To verify the biocompatibility of the modified Luers for the Cool Line, ICY, and Quattro Intravascular Heat Exchange Catheters, ZOLL conducted biocompatibility testing on the proximal (modified) portion of the catheter only. Similarly, to verify the biocompatibility of the modified SUK, ZOLL conducted biocompatibility testing on the SUK Custom Luers only. Biocompatibility testing was conducted in accordance with GLP regulations.

Because the Custom Molded Luer Set components located on the SUK and on the proximal end of the catheter only have indirect blood contact and prolonged exposure, ZOLL conducted testing based on the classification of an externally communicating device, blood path indirect for prolonged exposure (>24hrs and ≤30 days). Based on this classification, the following categories of biocompatibility tests were performed:

- Cytotoxicity
- Sensitization
- Irritation/Intracutaneous Reactivity
- Acute Systemic Toxicity

- Hemocompatibility

Test results are shown in **Table 7**.

Table 7. Biocompatibility Testing

Test Category	Test Method Summary	Results
Cytotoxicity	MEM Elution Test	The reactivity grade of all test article extract samples was "0".
Sensitization	ISO 10993 Part 10 Guinea Pig Maximization Sensitization Test (GLP)	The test article extracts did not cause sensitization reactions under the conditions of the assay.
Irritation	ISO/USP Intracutaneous Reactivity Irritation Test in Rabbits (GLP)	The data indicated that the test article extracts did not cause a skin irritation reaction.
Acute Systemic Toxicity	ISO/USP Medical Device Acute Systemic Toxicity Test in Mice (GLP)	Based on the clinical observations and body weight evaluations, the test article (device) extracts did not show significantly greater biological reaction than the control article extracts.
Material Mediated Pyrogen	ISO/USP Materials Mediated Pyrogen Test in Rabbits (GLP)	None of the animals in the study showed abnormal clinical signs prior to dose administration or during the observation period and no animals showed a temperature increase of 0.5°C or greater during the study period.
Hemocompatibility	ASTM Hemolysis (Extract Method) Test (GLP)	The difference between the hemolytic indexes of the test article and the negative control equals 0.00 percent. This places the test article in the non-hemolytic range. All test method acceptance criteria were met.
Hemocompatibility	Complement Activation Test (GLP)	**C3a:** The P value was >0.050 when the test article was compared to the predicate at the 30, 60, and 90 minute time points; the test article and predicate are statistically similar at these time points. The P value was >0.050 when the test article was compared to the negative control at the 30, 60, and 90 minute time points; the test article and predicate are statistically similar at these time points. **SC5b-9:** The P value was >0.050 when the test article was compared to the predicate at the 30, 60, and 90 minute time points; the test article and predicate are statistically similar at these time points.

Test Category	Test Method Summary	Results
		The P value was >0.050 when the test article was compared to the negative control at the 30 and 60 minute time points; the test article and negative control are statistically similar at these time points. The P value was ≤0.050 when the test article was compared to the negative control at the 90 minute time point; the test article is statistically lower than the negative control at this time point.

The results of the testing demonstrate that the modified SUK and the modified Cool Line, ICY, and Quattro Intravascular Heat Exchange Catheters are biocompatible for their intended use and the modifications made to the subject devices do not adversely affect the established biocompatibility of the predicate devices.

Usability/Human Factors

Pursuant to the FDA guidance document titled "Draft Guidance for Industry and Food and Drug Administration Staff - Applying Human Factors and Usability Engineering to Optimize Medical Device Design" Human Factors testing was conducted as follows:

1. **Summary of Formative Testing**
   Human factors formative testing was performed to determine if users trained according to the IFU can properly perform the following:
   - Identify infusion lumens, (proximal, medial, and distal)
   - Properly connect the IN and OUT Luers to the Start-Up Kit (SUK)
   - Identify the saline IN and OUT Luers
   - Identify any lumen that is appropriate for pharmacological infusate.
   - Disconnect the Saline IN and OUT track (SUK Luers) including evacuating the saline from the catheter using a syringe.

   User tasks were based on identifying and (or) making proper connections as documented in the Formative Human Factors Protocol for ZOLL Custom Luers. The test session ran over the course of two days.

   Four scenarios were presented, and participants were evaluated based on 14 predefined success metrics. All participants correctly executed each scenario, with no failures. All participants who received representative level of training and had access to the IFU successfully completed all of the tasks. This indicates that the device design, training content and the IFU adequately mitigate the risk of misconnections. No device design, training or IFU modifications were indicated based on this formative test.

2. **Summary of Summative Testing**

Human factors summative testing was performed to evaluate if users trained according to the ZOLL Custom Luer Training Program and IFU can properly perform the following:

- Match the new catheter and new Start-Up Kit (SUK) with custom Luers
- Place 20 cc syringe on saline hook on TGXP (Thermogard XP) console
- Connect the IN and OUT Luers on the catheter to its counterpart on the SUK
- Select an infusion lumen for an IV infusion
- Use 20 cc syringe for aspiration of saline after a catheter is used as a CVC after temperature management therapy ends
- Aspirate saline prior to catheter removal.

A total of five scenarios were presented, and each participant had to correctly answer questions 9-13 to achieve a passing score. All other questions (1-8, 14-15) required a minimum of an 80% passing score. The acceptance criteria were met with 100% of the users passing the critical tests (9-13). All of the non-critical items (1-8 and 14-15) were passed with at least 12 participants passing (80%).

All participants who received training and followed the IFU successfully met the acceptance criteria. This testing confirms that the custom Luer design, training, and IFU facilitate appropriate catheter and SUK connections. No device design, training or IFU modifications were indicated based on the summative evaluation.

V. Summary of Clinical Tests Performed

Clinical evaluations were not performed for the modified SUK and the modified Cool Line, ICY, and Quattro Intravascular Heat Exchange Catheters because such evaluations were not necessary to demonstrate substantial equivalence of the modified devices to the predicate devices (SUK: K014241; Catheters: K101987).

VI. Substantial Equivalence

The modified SUK and the modified Cool Line, ICY, and Quattro Intravascular Heat Exchange Catheters have the same intended use / indications for use as the 510(k) cleared SUK (K014241) and the 510(k) cleared Cool Line, ICY, and Quattro Intravascular Heat Exchange Catheters; Catheters (K101987). The results of the packaging validation (SUK only), bench performance, biocompatibility, and usability testing demonstrate that the modifications do not affect the performance or function of the devices. The minor differences in the design between the modified and cleared devices, do not raise any new types of safety or effectiveness questions as confirmed by design verification testing. Therefore, the modified SUK and the modified Cool Line, ICY, and Quattro Intravascular Heat Exchange Catheters are substantially equivalent to the previously cleared predicate devices.

VII. Conclusions

ZOLL concludes that based on the results of the packaging validation, bench performance, biocompatibility and usability testing performed, the modified SUK and the modified Cool Line, ICY, and Quattro Intravascular Heat Exchange Catheters are substantially equivalent to the predicate devices.