RD 12002
Design Validation of RTC 25-C Inline Aerosol Tee Adapter
April - September, 2013

Purpose:

The purpose of this testing is to validate the various mating fits associated with the RTC 25-C Inline Aerosol Tee Adapter components. These include the fits between: the tee and cap, the tee and insert, the tee with assembled insert and the Boehringer Ingelheim Respimat® medication delivery system, and the assembled tee adapter and the Fisher & Paykel RT240 ventilator circuit wye. Positive End Expiratory Pressure (PEEP) loss is also being quantified for RTC 25-C Adapter usage with a non-leak compensated ventilator.

Abstract:

The RTC 25-C Inline Aerosol Tee Adapter is a device being developed at Instrumentation Industries, Inc. under the project designation RD 12002. The device has been designed to enable the use of a new aerosolized medication delivery system within a ventilator circuit. Boehringer Ingelheim has begun utilizing a delivery system called the Respimat® for the medication Combivent®, a bronchodilator used for treating patients with chronic obstructive pulmonary disease (COPD). Combivent® used to be available in a Metered Dose Inhaler (MDI) canister and could be delivered to ventilator patients with the use of an inline MDI adapter, but the Combivent® MDI has been replaced by the Combivent® Respimat®. The RTC 25-C Inline Aerosol Tee Adapter is not an MDI adapter because it does not initiate activation of the medication or affect medication particle size. It serves only as a conduit for already-aerosolized medication to enter a ventilator circuit and should be usable for any medication that is deliverable with the Respimat® system.

The Risk Analysis for this device has identified the need to have a proper mating fit between the center port of the tee and the Respimat® medication delivery system. The cap also must have a secure fit on the center port of the tee. The fit between the tee insert and the center port of the tee is a tight interference fit by design. This fit is also being tested to ensure that the insert will not come loose due to circuit pressure or cap disassembly. The performance-related functionality tests include a visual check for aerosolized medication going toward the patient during dosage and a test for Positive End Expiratory Pressure (PEEP) loss during ventilator cycling.

Fit testing and/or dimensional inspection was performed on various molded component groups early in the project to determine good molding parameters for each component. Validation testing was then conducted with representative samples of components molded within the projected final parameter ranges. We feel confident in the consistency of the molded parts to this point, especially those molded within the projected parameter ranges.

Testing was split between April-May and September due to a design change that added the tee insert and removed a lug from one side of the tee. Similar testing was performed before and after the design changes and other additional tests were only performed after the changes due to a recognized need for a new test. Most of the testing was conducted by Steven Reiner. Brenda Blasinsky was present for a portion of the testing, primarily for the Usage tests, which verified that the Respimat® unit fit properly on the tee and that the medication was dispersing properly through the device and into the ventilator circuit.

Equipment Utilized:

Bear 3 Ventilator
Fisher & Paykel RT240 Ventilator Circuit
Meriam Instrument Smart Pressure Gauge (calibration due 5-31-14)
Various Molded RTC 25-C Adapter Components

Test Descriptions and Data:

Cap Fit - Ventilator Cycling Test (May, 2013)

Using a Tee from D0304113 and a Cap from samples molded on 4-23-13, an assembled RTC 25-C Adapter was placed inline and cycled on our in-house Bear 3 ventilator for several 6-8 hour sessions (during the work day). Testing was performed with various cap assembly conditions, including: cap and tee assembled dry, cap and tee assembled after running under cold water, cap and tee assembled after soaking in warm water for a few minutes, cap assembled after rubbing a little hand cream on the outside of elliptical tee port. Several times during the day, the bag was squeezed so that the volume was severely limited and the peak pressure would spike to simulate coughing or a similar event. The bag and tidal volume were changed to achieve varying peak pressures. The cap was removed from the tee port and reassembled 10-15 times prior to each day's cycling to simulate repeated use.

Date	Wet/Dry Assy	Breaths per Min.	Peak Prs. (cm H_2O)	PEEP (cm H_2O)	Intermittent Spikes (cm H_2O)	Results
4-24	Wet	8	~40	5	70-90	Good - Cap remained in place
4-25	Wet	8	~40	5	70-90	Good - Cap remained in place
4-26	Dry	8	~40	5	70-90	Good - Cap remained in place
4-29	Dry	8	~40	5	70-90	Good - Cap remained in place
4-30	Wet-warm	8	~40	5	70-90	Good - Cap remained in place
5-1	Dry	8	~40	5	70-90	Good - Cap remained in place
5-2	Hand cream	8	~40	5	70-90	Good - Cap remained in place
5-3	Wet-warm	8	~40	5	70-90	Good - Cap remained in place
5-6	Dry	8	~40	5	70-90	Good - Cap remained in place
5-7	Dry	12	~100	5	~120	Good - Cap remained in place
5-8	Wet	12	~100	5	~120	Good - Cap remained in place
5-9	Wet-warm	12	~100	5	~120	Good - Cap remained in place
5-10	Hand cream	12	~100	5	~120	Good - Cap remained in place

Cap Fit - Ventilator Cycling Test (September, 2013)

Using a Tee from D0900513, a Cap from D0403813, and aTee Insert sample molded on 9-9-13, an assembled RTC 25-C Adapter was placed inline and cycled on our in-house Bear 3 ventilator for three 6-8 hour sessions and one 13 hour session (on 9-11). Testing was again performed with various cap assembly conditions and with intermittent pressure spikes occasionally during the day. The bag and/or tidal volume were changed to achieve varying peak pressures. The cap was removed from the tee port and reassembled 10-15 times prior to each day's cycling to simulate repeated use.

Date	Wet/Dry Assy	Breaths per Min.	Peak Prs. (cm H_2O)	PEEP (cm H_2O)	Intermittent Spikes (cm H_2O)	Results
9-10	Wet	10	~40	5	70-90	Good - Cap and Insert remained in place
9-11	Dry	10	~50	5	70-90	Good - Cap and Insert remained in place
9-12	Wet-warm	20	~60	5	80-100	Good - Cap and Insert remained in place
9-13	Dry	20	~60	5	80-120	Good - Cap and Insert remained in place

Cap Fit – Static Pressure Tests (May, 2013)

Several static pressure tests were run using Tees molded on 3-28-13 from sample groups 4 and 6 (the projected high and low injection speed range) and Caps from D0403813. Input pressures of 8 psi or less were introduced using a plunger and a wall source was used for higher pressures. The calibrated Smart Pressure Gauge was used for the lower pressure tests. The gauge on the wall regulator was used for determining the approximate source pressure of the higher pressure testing. The source pressure and gauge were connected to one end of the tee and the other end was capped during testing.

Test #1: The outer elliptical walls were cut off the caps so that only the inner circular portion could obtain a mating fit with the tee. For this test, each of the four Cap cavities was mated with each of the two Tee cavities. The assemblies were subjected to an internal pressure of over 320 cm H_2O for 3 minutes. The pressure was held for over 30 minutes on one of the trials. Trials were repeated with the caps just snugged, not pushed on hard. Trials were repeated with a moderately snug fit at 5-6 psi for 2 minutes. A couple of trials were also repeated at over 8 psi for 2 minutes. Many of these trials were run both wet and dry.

Results: Good – none of the Caps popped off during any of the trials.

Test #2: This test utilized two groups of Caps from D0403813 – one molded with the projected maximum injection pressure and one molded with the projected minimum injection pressure. Each cap cavity was assembled onto each Tee cavity. The assemblies were subjected to an internal pressure of 5-6 psi for 2 minutes. Each of the trials was run both wet and dry.

Results: Good – none of the Caps popped off during any of the trials.

Test #3: This test utilized the same Tee Assemblies from test #2. The assemblies were subjected to an internal pressure of ~25 psi for 10-15 seconds. These trials were run with dry components.

Results: Good – none of the Caps popped off during any of the trials.

Test #4: This test utilized the Tee Assembly that had been actively running on the Ventilator Cycling Test. To this point (5-1), this Tee Assembly had run for 6 – 6+ hour ventilator sessions, with 10-15 disassembly/assembly cycles between sessions. Immediately after removing the Tee Assembly from the ventilator circuit, it was pressure tested at 5-6 psi. It was then soaked in hot water for 4-5 minutes and retested at 5-6 psi for 5 minutes. The cap was removed from the tee and reassembled with wet components and retested at 5-6 psi for 10 minutes. The cap was again removed from the tee and reassembled with wet components and retested at 5-6 psi for 15 minutes.

Results: Good – none of the Caps popped off during any of the trials.

Cap Fit – Static Pressure Tests (September, 2013)

Using Tees from D0900513 (two weeks old at the time) and D0902913 (2 days old at the time), Caps from D0500313 (first completely acceptable production lot), and Inserts molded on 9-17-13 (3 days old at the time) from groups molded at 1100 psi (projected minimum injection pressure) and 1000 psi (below projected minimum injection pressure), several tests were run as follows. 48 Tee Assemblies were created with the components equally distributed by cavity – Tee (2), Cap (4), and Insert (2).

Test #1: Used dry Tee Assemblies with Cap on. 24 of the samples were subjected to an internal pressure of 5-6 psi for 2 minutes.

Results: Good – none of the Caps popped off during any of the trials.

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Test #2: Assembled and disassembled the Cap and Tee 50 times. The cap was pulled off quickly to achieve a popping sound from the vacuum. This served as a test to see if the insert would move or become dislodged. After the Cap was assembled for the 50th time, test #1 was repeated (5-6 psi for 2 minutes). The remaining 24 Tee Assemblies were used for this test.

Results: Good – none of the Caps popped off during any of the trials.

Test #3: Using the same group of 24 Tee Assemblies from test #2, the samples were soaked in hot/warm water for at least 5 minutes prior to testing. Warmer water was added occasionally to keep the water bath from getting cold. Each of the Tee Assemblies was tested again at 5-6 psi for 2 minutes.

Results: Good – none of the caps popped off during any of the trials.

Insert Fit – Static Pressure Tests (September, 2013)

Using the same group of 24 Tee Assemblies from Cap Fit Static Pressure Test #1, two tests were conducted to ensure a secure press fit of the Insert within the Tee. The setup was similar to the Cap Fit Static Pressure Tests, with the source pressure at one tee port and the other end of the tee blocked off.

Test #1: The Cap was removed from the Tee port and a ~30 psi source was applied to the Tee for 10-15 seconds.

Results: Good – none of the Inserts moved or became dislodged during any of the trials.

Test #2: Using the same group of Tee Assemblies, the inserts were removed and replaced 5 times. Final assembly took place with warm, wet components. Test #1 was repeated (~30 psi source for 10-15 seconds).

Results: Good – none of the Inserts moved or became dislodged during any of the trials.

Usage Test (May, 2013)

Each of two Tees from D0304113 (one of each cavity) were placed in the inspiratory limb of a ventilator circuit at the wye. The ventilator was cycled with a breathing bag serving as the patient. The Respimat® unit was seated firmly on the adapter and multiple doses of placebo medication were introduced inline. For each trial, the medication suspended inside of the Tee until the inhalation cycle took it straight to the patient. A slight amount of aerosolized medication leaked through the dosing button on the Respimat® unit, but none appeared to leak out of the air entrainment holes on the unit.

Results: Good – the Respimat® unit fit on the elliptical Tee port properly and the aerosolized medication dispersed as intended, except for a small leak out of the dosing button.

Usage Test (September, 2013)

Four Tee Assemblies containing each of the two Tee cavities and each of the two Insert cavities that were previously used for Static Pressure Testing were used for this test. Each Tee was placed in the inspiratory limb of a ventilator circuit at the wye. The ventilator was cycled with a breathing bag serving as the patient. The Respimat® unit was seated firmly on the adapter and multiple doses of placebo medication were introduced inline. For each trial, the medication suspended inside of the Tee until the inhalation cycle took it straight to the patient. None of the medication appeared to leak out of the dosing button or air entrainment holes on the Respimat® unit.

Results: Good – the Respimat® unit fit on the elliptical Tee port properly and the aerosolized medication dispersed as intended without any apparent leaks.

PEEP Loss Test (May, 2013)

A test was performed using two prototypes and a regular Tee Assembly to establish a baseline reading. The prototype Tees were machined to create a ledge down inside the center port where machined Inserts were pressed. One of the inserts had a Ø.052 orifice and the other had a Ø.0625 orifice. This test was performed to see how big of an orifice that we could get away with without affecting Positive End Expiratory Pressure (PEEP) significantly. This test was performed with our in-house Bear 3 ventilator. Tidal volume was adjusted to achieve various peak pressure readings. Each trial grouping shown was tested at the same ventilator settings. The peak pressure varied due to volume loss out of the Insert orifice in the prototypes. Peak Flow was set at 60 LPM, but specific Tidal Volume settings and Rate were not recorded.

Tee Description	Approx. Peak Pressure (cm H_2O)	PEEP Start (cm H_2O)	PEEP End (cm H_2O)	PEEP Loss (cm H_2O)
RTC 25-C (capped)	30	4½	6	0
Tee Prototype w/ Ø.052 orifice	23	5½	4	1½
Tee Prototype w/ Ø.0625 orifice	22	6	3½	2½
RTC 25-C (capped)	37	3½	4¾	0
Tee Prototype w/ Ø.052 orifice	32	3½	3	½
Tee Prototype w/ Ø.0625 orifice	29	3½	2½	1
RTC 25-C (capped)	43	3½	4¾	0
Tee Prototype w/ Ø.052 orifice	36	3½	3	½
Tee Prototype w/ Ø.0625 orifice	34	3½	2½	1
RTC 25-C (capped)	50	5	6¾	0
Tee Prototype w/ Ø.052 orifice	44	5	4½	½
Tee Prototype w/ Ø.0625 orifice	41	5	3½	1½

Results: Good for the prototype with the Ø.052 orifice Insert and not as good for the prototype with the Ø.0625 orifice Insert. There is not a definitive pass/fail number for this test, but we were looking for a PEEP loss of 2 cm H_2O or less throughout the whole range of Peak Pressures. This test helped us to make the decision to specify a Ø.052 orifice in the molded Insert.

PEEP Loss Test (September, 2013)

Two Tee Assemblies containing each of the two Insert cavities that were previously used for Static Pressure Testing were used for this test. This test was performed with our in-house Bear 3 ventilator. Tidal volume was adjusted to achieve various peak pressure readings. Each trial grouping shown was tested at the same ventilator settings. The peak pressure varied due to volume loss out of the Insert orifice in the uncapped Tees. Ventilator Settings: Tidal Volume varied from .75L to 1.8L with 3L bag, Peak Flow = 60LPM, Rate = 10 BPM

Tee Description	Approx. Peak Pressure (cm H_2O)	PEEP Start (cm H_2O)	PEEP End (cm H_2O)	PEEP Loss (cm H_2O)
Capped Tees (both had same results)	30	4	6	0
Uncapped Tees (both had same results)	24	4	2	2
Capped Tees (both had same results)	36	4	6	0
Uncapped Tees (both had same results)	32	3½	2	1½
Capped Tees (both had same results)	41	4	6	0
Uncapped Tees (both had same results)	36	3½	2½	1
Capped Tees (both had same results)	45	4	6	0
Uncapped Tees (both had same results)	42	4	3½	½

Results: Good, due to the fact that we met our initial goal of 2 cm H2O or less for the range of Peak Pressures tested. The results do not exactly match the results from the initial test in May. This is likely due to the two tests being conducted at different respiratory rates (unfortunately, we did not record the rate during the initial testing). Using a ventilator without leak compensation (like our Bear 3), there will be more PEEP loss with a lower respiratory rate because the pressure has more time to leak out. Our external R.T. consultant on this project, Jim Roth, and his boss (a director of Respiratory Care at UPMC hospital) thoroughly tested production-equivalent samples in September and found that there was no PEEP loss at all throughout the entire range of PEEP settings using a modern ventilator with leak compensation.

Circuit Wye Fit Check (September, 2013)

Tee Assemblies containing both of the Tee cavities were assembled onto a Fisher & Paykel RT240 Ventilator Circuit Wye on the inspiratory side. Both Tee Assemblies fit without interference. Jim Roth also was satisfied with the fit after the one lug was removed from the side of the Tee to address his original concern about the mating fit with that particular Wye.

Results: Good – the Tee Assemblies fit onto the wye as intended.

Summary of Results:

These testing trials were conducted to validate all of the mating fits associated with the RTC 25-C Inline Aerosol Tee Adapter components. These include the fits between: the tee and cap, the tee and insert, the tee with assembled insert and the Boehringer Ingelheim Respimat® medication delivery system, and the assembled tee adapter and the Fisher & Paykel RT240 ventilator circuit wye. Positive End Expiratory Pressure (PEEP) loss is also being quantified for RTC 25-C Adapter usage with a non-leak compensated ventilator.

The cap fit on the tee port was validated by running several tests. Two rounds of in-house ventilator cycle testing were performed over a total of 17 days. Many hours of cycling was done at very elevated peak pressures – up to 100+ cm H_2O. Occasional pressure spikes (at up to 120 cm H_2O) were introduced several times per day to simulate a patient coughing or a similar event. The cap was removed and replaced 10-15 times every morning, prior to cycling, to simulate repeated use. Throughout the course of the ventilator cycle testing, the cap never became dislodged. In use, the device should regularly experience typical peak pressures of less than 40 cm H_2O. The ventilator cycling testing was performed with 40 cm H_2O as a starting point. We are satisfied that the device was subjected to sufficiently demanding conditions during this test.

Two rounds of static pressure testing were also done on the cap fit. These were conducted in various conditions, including those with dry components, wet components, wet and warm components, and even caps with the elliptical outer walls cut off (meaning only the circular port was providing all of the sealing and holding power). We originally specified pressure testing up to 160 cm H_2O because these devices probably will never experience pressures over 120 cm H_2O. Early on, however, when it seemed that 160 cm H_2O would be easy criteria to meet, the testing pressure was doubled to over 320 cm H_2O as an added measure of security. Various trials were also run at internal pressures of up to 8 psi. None of the caps became dislodged during any of the testing trials.

The insert fit within the tee port was validated with two static pressure tests. We originally specified pressure testing with a source of 5 psi to be consistent with some of the cap static pressure testing. However, since the insert has an open orifice, we decided to increase the pressure significantly to increase the back pressure behind the insert. As a result, both tests used a 30 psi source. The second test also added warm, wet components combined with repeated assembly and disassembly of the insert prior to testing. These components are not intended to be disassembled at all, so this was a very stringent test. The inserts did not move or become dislodged during any of the trials of either test. Since the device should never see a source pressure of anything higher than ~2 psi, we are satisfied with the fit of the assembled insert within the tee port.

A secondary validation test of the insert occurred during the cap static pressure testing trials. One of these tests required that the cap be pulled off each tee port very fast 50 times. During a fast removal, a popping sound is

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created by the vacuum, which should try to pull the insert out of the tee port. None of the inserts moved or became dislodged during any of these trials.

Two rounds of testing were conducted to demonstrate that the Respimat® medication delivery system fits properly on the tee port and medication disperses as intended through the device. Both testing trials utilized a patient circuit with a cycling ventilator so that the medication could be seen traveling towards the breathing bag (patient). The Respimat® unit fit onto the tee port snugly and was able to be easily pressed down far enough on the port to block the air entrainment ports on the sides of the unit and to allow good dispersion of the medication through the tee insert orifice. Both rounds of testing were successful.

Two PEEP loss tests were conducted with a cycling Bear 3 ventilator. This is an old ventilator that does not have leak compensation, which is important to completely eliminate PEEP loss. The RTC 25-C device has an internal orifice that will allow a leak while the cap is off. Depending on the settings, when used with a non-leak compensated ventilator, the device will likely allow a small PEEP loss. The Respiratory Rate definitely affects the amount of PEEP loss. As the rate decreases, the PEEP loss increases. We were hoping to see a PEEP loss of 2 cm H_2O or below throughout the range of settings tested and we did meet this goal. The typical PEEP loss was 1½ cm H_2O or less, but one of the trials showed a 2 cm H_2O loss. Overall, we considered this to be a successful test.

Our external R.T. consultant on this project, Jim Roth, and his boss, a Director of Respirator Care at a UPMC hospital, performed a series of tests on production-equivalent samples of the RTC 25-C Adapter. Jim's conclusion was that the RTC 25-C causes a very temporary tidal volume loss immediately after the cap is removed, but it recovers right away. He said that they tested the device at several PEEP settings, all the way up to 20 cm H_2O and his conclusion is that there is no PEEP loss at all. He was very adamant about that. His testing was performed on a modern ventilator with leak compensation, which the vast majority of users will have. We decided to put a caution in the user instructions that a loss of tidal volume and PEEP may occur when the cap is removed from the tee. Overall, we are satisfied with the device with respect to PEEP loss.

The device was officially fit-tested with the Fisher & Paykel RT240 ventilator circuit wye on the inspiratory side. This was the popular circuit wye that Jim Roth told us did not mate properly with the device back in June. Our testing showed that the RTC 25-C now mated fine with the wye since we eliminated one of the lugs from the side of the device.

Finally, looking through the inspection records for all of the molded components in this project, all of the fit checks conducted as part of the QC lot inspections were successful. These include cap to tee, insert to tee, and Respimat® unit to tee.

Conclusion:

All of the in-house validation testing conducted for the RTC 25-C Inline Aerosol Tee Adapter was successful. The device was also repeatedly evaluated by an external Respiratory Therapist and a Director of Respiratory Care. Their opinion is that the device is well-designed and ready for its intended use. The device appears to be safe and effective and we will be releasing the device for sale with the completion of all of the necessary documents. These include the Final Review in project RD 12002 and all of the production documents being created through ECO 2187.

Approval of Validation Test Report for new RTC 25-C Inline Aerosol Tee Adapter in RD 12002:

President: Edward C. Huey 9-30-13 QA/RA: Doris F. Hatter 9/30/13

Engineering: Steven C. Reimer 9/30/13 Sales/Mktg: [signature] 9/30/13

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