

**DE NOVO CLASSIFICATION REQUEST FOR
RETROGRADE INTUBATION SET**

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Retrograde intubation device. A retrograde intubation device is a prescription device used to perform retrograde intubation via the cricothyroid membrane. The device may contain or be labeled for use with guidewires and intubating catheters, in addition to needles (21 CFR 868.5090), syringes (21 CFR 880.5860), and hemostats (21 CFR 878.4800).

NEW REGULATION NUMBER: 21 CFR 868.5095

CLASSIFICATION: Class II

PRODUCT CODE: QCX

BACKGROUND

DEVICE NAME: Retrograde Intubation Set

SUBMISSION NUMBER: DEN170055

DATE DE NOVO RECEIVED: September 25, 2017

CONTACT: Cook Incorporated
750 Daniels Way
Bloomington, Indiana 47404

INDICATIONS FOR USE

The Retrograde Intubation Set is indicated as follows:

The Retrograde Intubation Set is intended to assist in intubation during difficult or emergency airway access procedures in adult and pediatric patients.

The 6 French catheter is recommended for use with a single-lumen endotracheal tube with an inner diameter of 2.5 mm or larger.

The 11 French catheter is recommended for use with a single-lumen endotracheal tube with an inner diameter of 4 mm or larger.

The 14 French catheter is recommended for use with a single-lumen endotracheal tube with an inner diameter of 5 mm or larger.

When used for high pressure oxygenation with a Luer Lock connector, the 14 French catheter is recommended for patients older than 12 years of age.

LIMITATIONS

The sale, distribution, and use of the Retrograde Intubation Set are restricted to prescription use in accordance with 21 CFR 801.109.

When used for high-pressure oxygenation with a Luer lock connector, the 14 French catheter is recommended for patients older than 12 years of age.

This product is intended for use by clinicians trained and experienced in retrograde intubation techniques. Standard techniques for retrograde intubation should be employed.

This device is limited to use in hospitals, surgical centers, and acute care centers.

PLEASE REFER TO THE LABELING FOR A COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

DEVICE DESCRIPTION

The basic components included in the subject device, the Retrograde Intubation Set, are an introducer needle, catheter needle, syringe, hemostat, wire guide with wire guide inserter, intubation catheter, and Rapi-Fit® adapter. While the wire guide, intubation catheter, and Rapi-Fit® adapters are the subject of this De Novo request, this device is intended to be used with legally marketed needles, syringes, and hemostats.

The needle and syringe are used to puncture the patient cricothyroid membrane and confirm needle placement in the patient airway. Then, a wire guide is inserted via the needle into a patient's trachea and exits via mouth or nose (i.e., retrograde). An intubating catheter is inserted orally or nasally over the wire guide into the trachea prior to intubation.

This device offers optional Rapi-Fit adapters (attached to the intubating catheter) to facilitate supplemental oxygen delivery in adults prior to intubation with an endotracheal tube (ETT).

This device is comprised of the following components:

Introducer Needle (legally marketed under 21 CFR 868.5090, K160200):

The cannula of the introducer needle is 18 Gauge, 5 centimeters (cm) long, and made of stainless steel. The cannula tip is a Lancet bevel. Its primary function is to puncture the cricothyroid membrane in order to provide access for wire guide placement.

Catheter Needle (legally marketed under 21 CFR 868.5090, K160200):

The catheter needle is a hubbed catheter sheath covering a hubbed needle. The cannula of the catheter needle is 18 Gauge, 5 cm long, and made of Stainless Steel. The cannula tip is a Lancet bevel. The catheter sheath material is radiopaque fluorinated ethylene propylene. Its primary

function is to puncture the cricothyroid membrane in order to provide access for wire guide placement. Either the introducer needle or catheter needle can be used for wire guide placement, based on physician preference.

Syringe (legally marketed under 21 CFR 880.5860, K160200):

The 6 milliliter (mL) syringe is attached to the proximal end of the needle. It is used to confirm that the needle tip is located inside the trachea by aspirating air from the trachea.

Hemostat (legally marketed under 21 CFR 878.4800):

The stainless steel hemostat is used to clamp the wire guide near the entry point to stabilize the wire guide in the trachea.

Wire Guide and Wire Guide Inserter (is a subject of this De Novo request):

The wire guide's outer diameter is 0.038 inches and its length is 110 cm. The wire guide is also double, flexible tipped and includes a safety wire and a centerless ground mandril wire. The wire guide has a flexible 3 millimeter (mm) curve radius on the distal end and a flexible straight tip on the proximal end. Position markers are etched on the wire guide (0.5 ± 0.2 cm wide), both of which are 20 ± 1 cm away from the proximal and distal tips. The wire guide inserter is preloaded onto the distal end of the wire guide to assist insertion of the wire guide tip into the needle.

Intubation Catheter (is a subject of this De Novo request):

The yellow polyurethane catheter has an outer diameter of 14 French (Fr) and a length of 70 cm. It has incremental markings printed on the catheter shaft and six sideports at the distal end. There are labeled incremental markings evenly spaced at 5 cm, 10 cm, 15 cm, 20 cm, 25 cm, 30 cm, and 35 cm. Between the labeled markings are non-labeled marks with 1cm increments. The polyurethane catheter set also includes two Rapi-Fit adapters (one with a 15 mm connector and one with a Luer lock connector) for ventilation when oxygen requirement is high and the endotracheal tube has not been successfully placed within the tracheal space. The 15 mm Rapi-Fit adapter is intended for attachment to traditional ventilator sources that are low pressure sources, or so-called continuous positive airway pressure (CPAP) ventilators. The Luer Lock Rapi-Fit adapter is intended for attachment to a high pressure jet ventilation oxygen source. The Luer Lock connection is an ISO 594-2 compliant male Luer Lock, which is compatible with a variable connector or the standard Luer fitting of an oxygen tube which is connected to an oxygen source.

A black polytetrafluoroethylene (PTFE) catheter is also available in a diameter of 6 Fr and length of 50 cm or a diameter of 11 Fr and length of 70 cm. It has no markings or sideports. The PTFE catheter set does not have any Rapi-Fit adapters and is not designed for oxygenation.

Rapi-Fit Adapters (is a subject of this De Novo request):

The device set with a 14 French intubation catheter includes two Rapi-Fit adapters to be used for oxygenation for adults only. During intubation, in some cases, the requirement for oxygen can be high and the endotracheal tube has not been placed within the patient's tracheal space. The 14 Fr catheter set includes two Rapi-Fit adapters (one with a 15 mm connector and one with a Luer lock connector) to be used with oxygen sources.

Both adapters include an adapter body and a locking ring. The adapter body is attached to the proximal end of the intubation catheter to allow oxygenation using standard ventilation equipment if necessary during an intubation procedure. A locking ring locks the adapter body to the proximal end of the catheter for securement; it does not contact the patient during use. The 15-mm Rapi-Fit adapter is designed to be attached to traditional ventilator sources that are low pressure sources, or so-called continuous positive airway pressure (CPAP) ventilators. The Luer Lock Rapi-Fit adapter is designed to be attached to a high pressure jet ventilation oxygen source.

SUMMARY OF NONCLINICAL/BENCH STUDIES

BIOCOMPATIBILITY/MATERIALS

A biological risk assessment was performed and found to be in accordance with FDA guidance: *Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process* (issued June 16, 2016) for a device with limited duration contact (≤ 24 hours) with tissue/bone/dentin.

The sponsor evaluated biocompatibility per ISO 10993 (and its subparts) based on contact classification per the cytotoxicity (ISO 10993-5), sensitization (ISO 10993-10), irritation (ISO 10993-10), acute systemic toxicity (ISO 10993-11), and material-mediated pyrogen testing on the patient-contacting components of the subject device (catheters, wire guide, and Rapi-Fit adapters).

The methods for extractions were acceptable based on the FDA biocompatibility guidance (referenced above) given the intended use of the device. Based on the submitted testing and evaluations, the Retrograde Intubation Set mitigates biocompatibility concerns.

SHELF LIFE/STERILITY

The Retrograde Intubation Set is provided sterile and intended for single use. Ethylene Oxide (EO) sterilization validation was conducted on a representative worst case via the overkill approach at a sterility assurance level (SAL) of 10^{-6} in accordance with ISO 11135-1 :2007, *Sterilization of Health Care Products - Ethylene Oxide - Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices*. The worst-case sample is a stylet within an intubating catheter, which has the greater chance of inhibiting sterilization effectiveness compared to the final finished device. In the Retrograde Intubation Set, the catheter and guide wire are separated, leaving open pathways for sterilant to clear out. Sterilant residuals per ISO10993-7 are acceptable.

The final finished device package consists of the intubation catheter placed in the bottom of the universal tray. The Catheter Needle and Introducer Needle are placed into a Tyvek pouch and placed into the wells of the tray. The wire guide is packaged in a holder with a poly band and set into the bottom of the tray. The Rapi-Fit adapters are placed in the respective well (only applicable for the 14 Fr model of the subject device). The needle

holder is added to the tray in its well. The top tray and the bottom tray are held together between two white grips. The entire tray is then placed into an outer pouch, sealed, sterilized, and placed into a corrugated shipper prior to shipping.

A shelf-life claim of (b) (4) is supported with data for finished device (packages) that underwent 5 year accelerated aging (in accordance with ASTM F1980 - Standard Guide for Accelerated Aging of Sterile Medical Device Packages). Visual inspection, seal strength testing (in accordance with ASTM F88-09), and dye penetration (in accordance with ASTM F1929-12) test methods and results are acceptable to support a shelf life claim of (b) (4)

PERFORMANCE TESTING - BENCH

Tensile Testing (Shaft and Sideport):

The 6, 11, and 14 Fr catheters were tested for tensile strength per EN/ISO 10555-1:2013, Intravascular catheters — Sterile and single-use catheters — Part 1: General requirements. Prior testing of intubation catheters withdrawn from an ETT suggests that the highest force experienced by all test articles during withdrawal is approximately 12 Newtons (N). Although the scope of EN/ISO 10555-1:2013 does not encompass the subject device intubation introducers, the 15 N requirement is larger than the tensile force that would likely be experienced in the clinical environment. The 6 and 11 Fr catheters demonstrated tensile strength greater than the acceptance criterion along the catheter. The 14 Fr catheter met tensile strength acceptance criterion along the catheter and at the sideport.

Separation Force with Rapi-Fit adapter

The Rapi-Fit adapter separation force acceptance criterion was adopted from the tensile strength criterion (above). The adapters demonstrated separation forces greater than 15 N to mitigate the risk of disconnection. This testing is adequate.

Rapi-Fit Adapter Testing:

Testing was performed to verify the connectivity specifications of the Luer Lock and 15 mm hub on the adapters. The Luer Lock connector was tested in accordance with ISO 594-2 and the 15 mm connector was tested in accordance with ISO 5356-1:2015, Anaesthetic and respiratory equipment-Conical connectors-Part 1: Cones and sockets. The methods and results are acceptable.

Kink Radius Testing:

For the 6 and 11 Fr catheters, the acceptance criteria are based on the analysis of airway anatomy and the potential curvature of the exchange/intubation catheter in the airway, the worst-case inner curve radius of the catheter is approximately 48.17 mm for adult patients and 19 mm for pediatric patients. This acceptance criterion appears appropriate clinically. Because these two catheters are not intended to be used with oxygenation, the evaluation of the patency of the catheters when kinked is less important. Kinking could cause some difficulty in passing an endotracheal tube, but this is a known issue with antegrade intubation over a stylet or catheter. For this reason, the method of evaluating the 14 Fr

catheter (intended to be used with oxygenation) was conducted in accordance with Annex H of AAMI/ISO 5361:2012. The methods appear acceptable and all samples met the stated minimally acceptable kink radius criteria.

Radiopacity Testing:

Radiopacity was evaluated using the methods described in ASTM F640-12, Standard Test Methods for Determining Radiopacity for Medical Use. The methods appear acceptable and the results validate the radiopacity of the device compared to the reference material (aluminum).

Corrosion, Tensile, Flex, and Fracture Testing:

The guide wire was subjected to corrosion, tensile strength, flex, and fracture testing in accordance with ISO 11070, Sterile single-use intravascular introducers, dilators and guidewires.

During the corrosion test there were visual signs of corrosion on the wire guide; however, after the corrosion test, the same wire guide test articles underwent tensile testing in accordance with Annex H of BS EN ISO 11070. The peak load preceding failure was greater than or equal to 10 N for each test article. This validates that the wire guide is still able to perform as intended although it did show signs of corrosion after 3 years.

During fracture testing, each test article was only subjected to 3 complete turns (a deviation from the 8 recommended by ISO 11070) given that the typical clinical use of the device should not exceed a 90° bend. This methodology has been accepted for similar legally marketed guide wires and remains acceptable for this wire, given the typical clinical use.

The corrosion, tensile, flex, and fracture testing method and results are acceptable.

Validation Testing on Retrograde Intubation:

This testing was performed using a child and adult airway model to establish objective evidence that the finished device achieves its intended use. For each sample device, the operator followed the steps in accordance to the user manual of the Retrograde Intubation Set, which describes the retrograde intubation in two distinct stages, (1) obtaining access to the patient's airway through the cricothyroid membrane, and (2) oral or nasal intubation of the patient through access established in Stage 1. It is noted that the child manikin model does not have an option to simulate percutaneous tracheostomy, and therefore can only be used to evaluate Stage 2. However, the adult model can be used to represent the child model as the risks associated with puncturing the cricothyroid membrane with the needle are the same. The intubation catheters were able to support the intubation of both a child and adolescent model with endotracheal tubes ranging from 2.5 mm to 6.5 mm.

High Pressure Oxygenation Testing:

The Luer Lock connector was used as the worst case scenario, because it can facilitate ventilation at higher pressures between the two adapters, resulting in greater potential

harm (e.g., barotrauma, pneumothorax). In the child model (> 2 years to 12 years), some test articles of the 14 Fr intubation introducer of the subject device had an average maximum airway pressure greater than 28 cm H₂O. Given such high pressures (for the specific pediatric population), it was concluded that the oxygenation feature on the 14 Fr intubation catheter with Luer Lock Rapi-Fit adapter is not permissible in patients aged less than or equal to 12 years old. With this exception in this specific pediatric patient population, the remaining results are acceptable.

14 French Catheter Marking Accuracy

The 14 Fr catheter offers markings between 5 and 35 cm. Samples of the catheter are measured to validate labeled markings (every 5 ± 0.5 cm) and non-labeling increments (1 ± 0.2 cm) between each 5 cm mark. The maximum and minimum distance between each labeled mark is 5.1 and 5.0 cm (respectively), which is within specifications. The non-labeled marks were measured to be 1.0 cm for all samples tested. The results are acceptable.

SUMMARY OF CLINICAL INFORMATION

The subject device is intended to provide emergency invasive airway access using a technique listed in the American Society of Anesthesiologists Practice Guidelines for Difficult Airway Management. This technique was first described in the 1960s; a retrograde intubation kit, similar to the subject device, was commercially available at that time. Since then, other devices and techniques (e.g., laryngeal mask airway, video laryngoscopes) has decreased the need for rescue techniques such as retrograde intubation. This rarely performed rescue technique is performed in emergency situations and not readily amenable to a clinical study. The best evidence of safety and effectiveness comes from real world experience reported in the literature. The most comprehensive review was published by Sanchez in 1993 (Sanchez AF; The retrograde cookbook, Irvine, 1993, University of California). This publication also summarizes all known case reports and case series of retrograde intubations up to 1993. The Sanchez summary describes the techniques, indications, contraindications, complications, and failures associated with this technique. The effectiveness was quite high with an overall failure rate of only 2.2% (12 of 539 patients).

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In regard to safety of the device, the same database of 539 procedures (Sanchez) documented relatively few complications, and most were self-limited.

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Review of the literature after 1993 does not reveal any new safety signal for this technique or change in effectiveness for the technique. This evidence is applicable to the safety and effectiveness of the subject device because the technique is the same with an additional capability of oxygenating through the catheter when needed.

Pediatric Extrapolation

In this De Novo request, existing clinical data was leveraged to support the reasonable assurance of safety and effectiveness of the proposed device in pediatric patients.

As previously stated in the Summary of Clinical Information section, this technique dates back to the 1960s and since then, new techniques were developed that minimize the use of retrograde intubation. Given it is not a candidate for clinical trials and the lack of additional literature to report adverse events different than what is reported by Sanchez, this same literature was used to support safety and effectiveness of the device for pediatric populations. Thirty of 539 patients documented in this literature are pediatric patients, with the youngest patient being one day old. The safety and effectiveness in the pediatric subgroup was not significantly different, although the numbers are relatively small.

The technique used with the subject device is the same as described in the supporting literature for adult and pediatric patients, although a higher incidence of difficulties has been reported in the pediatric patient due to the characteristic differences in pediatric glottic anatomy and the association of difficult airways with congenital anomalies. Sanchez cites literature suggesting that retrograde intubations in pediatric patients with congenital anomalies may be more successful when combined with other techniques such as direct laryngoscopy or fiberoptic scope (Audenaert et al, *Anesth Analg* 73:660, 1991). While clinicians may consider this information during use, we reiterate that this device is intended for airway rescue where the alternative is death. Therefore, the incidence of difficulties in pediatric populations does not outweigh the benefit of potential intubation facilitated by this device as labeled.

The device is sized appropriately for the full range of pediatric endotracheal tubes, and the intubating catheters are labeled to show compatibility with respective endotracheal tube sizes. The capability to oxygenate through the intubating stylet is not indicated for subjects less than 12 years of age, as the risk for barotrauma is higher in this population.

LABELING

Given this procedure is used in critical patients that are difficult to intubate and ventilate, the labeling facilitates use of this device by (1) instructing the user on proper procedures for use and (2) specifying on the final finished package label the minimum compatible size of endotracheal tube that can fit over the included intubating catheter.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of the retrograde intubation device and the measures necessary to mitigate these risks.

Identified Risks to Health	Mitigation Measures
Failure to intubate and ventilate (continued hypoxia)	Non-clinical performance testing Labeling
Tissue damage/trauma resulting in, for example: <ul style="list-style-type: none">• Bleeding, hematoma• Subcutaneous emphysema• Pneumomediastinum or pneumothorax• Damage to trachea, esophagus, and vocal cords	Non-clinical performance testing Labeling
Infection	Sterilization validation Shelf-life testing
Adverse tissue reaction	Biocompatibility evaluation

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the retrograde intubation device is subject to the following special controls:

- (1) Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use, including the following:
 - A. Wire guide tensile, flex, fracture, and corrosion testing;
 - B. Catheter tensile strength testing at likely points of failure;
 - C. Catheter kink radius testing;
 - D. Compatibility of device components that interact, including compatibility in connection, disconnection, and ability to transfer fluids;
 - E. Dimensional validation;
 - F. Accuracy testing of markings;
 - G. Validation of the maximum airway pressure.
- (2) Performance data must support the shelf life of the device by demonstrating continued sterility, package integrity, and device functionality over the identified shelf life.
- (3) The device must be demonstrated to be biocompatible.
- (4) Labeling must include:
 - A. Instructions for use; and

- B. Package labels that clearly identify the minimum compatible size of endotracheal tube.

BENEFIT-RISK DETERMINATION

The risks of the device are based on data collected in the clinical literature described above. The risks associated with the use of the device include continued hypoxia (failed intubation, including esophageal intubation) and/or tissue damage/trauma (damage to blood vessels, the trachea or esophagus, the larynx (including vocal cords), pharynx, oral or nasal mucosa, which may result in adverse events such as, but not limited to: bleeding and hematoma, subcutaneous emphysema, pneumomediastinum or pneumothorax). The probability of these outcomes occurring as a result of the device use is moderate and dependent on the experience and training of the user. These risks are mitigated by adequate instructions for use (including adequate sizing). In addition, these risks are mitigated by non-clinical testing to confirm valid specifications and device components interactions. This device may also cause infection or adverse tissue interactions. These risks are mitigated by sterility and biocompatibility and validations.

The benefits associated with the device outweigh the risks. These probable benefits of the device are based on data collected in the clinical literature as described above. The subject device facilitates a lifesaving technique for patients in “cannot intubate cannot ventilate” situations. The subject device may provide an alternative to more invasive techniques such as cricothyrotomy or tracheotomy. The retrograde intubation technique has been a longstanding essential element in specific situations such as blood in the airway, trismus, congenital abnormalities, limited mouth opening, bone and joint disorders such as rheumatoid arthritis or ankylosing spondylitis, and failed intubation.

Patient Perspectives

This submission did not include specific information on patient perspectives for this device.

Benefit/Risk Conclusion

The intended use of this device is for airway rescue in emergent situations where the alternative is death. The data provided demonstrate the probable benefits of this device for its intended use and the probable risks can be mitigated by the use of general controls and the identified special controls. Therefore, we believe the clinical evidence, in combination with the appropriate labeling, supports safe and effective use of the device for emergency airway access by clinicians trained in emergency airway management.

CONCLUSION

The De Novo request for the Retrograde Intubation Set is granted and the device is classified as follows:

Product Code: QCX
Device Type: Retrograde intubation device
Class: II
Regulation Number: 21 CFR 868.5095