



Critical Care Therapy and Respiratory Care Section

Category:	Clinical
Section:	Medicinal Gas Therapy
Title:	Nitric Oxide Therapy
Policy #:	02
Revised:	05/00

1.0 PROCEDURE: Nitric Oxide delivery via the Ohmeda INOvent delivery system in mechanically ventilated patients.

2.0 DEFINITION/DESCRIPTION

Nitric Oxide (NO), not to be confused with the anesthetic nitrous oxide, is a gas molecule with selective vasodilation properties. NO is the active metabolite of a number of other vasodilators, including sodium nitroprusside and nitroglycerin. It is also produced in all human organ systems, including the nasopharynx and lungs. In high concentration, NO is profoundly toxic and causes disease identical to Acute Respiratory Distress Syndrome (ARDS). In the presence of oxygen, NO is broken down to form nitrogen dioxide (NO₂). In the blood NO interacts with hemoglobin. The byproduct of this reaction produces increased levels of methemoglobin. Methemoglobin will not carry oxygen, and therefore, its level must be closely monitored during NO therapy.

Inhaled NO provides selective vasodilation of the pulmonary arterioles without systemic effect. Vasodilation of the pulmonary arterioles will provide a decrease in pulmonary vascular resistance (PVR) which should improve blood flow to the lung.

The **INOvent delivery system** is an integrated, single unit, designed to administer and monitor inhaled NO. The INOvent delivery system connects to the inspiratory limb of the patient breathing circuit. It functions by measuring gas flow in the breathing circuit and injecting the required flow of NO to deliver the concentration set by the user in parts per million. It is designed to deliver a constant concentration of NO, independent of ventilator flow patterns.

3.0 SETTING

Inhalation of nitric oxide via the Ohmeda INOvent Delivery System will be performed in 10D ICU by personnel trained and competent in this procedure.

3.1 Administration of NO in the MICU

NO has been approved for use in the treatment of term or near term (> 34 weeks) neonates with hypoxic respiratory failure associated with clinical or echocardiographic evidence of pulmonary hypertension.

Obtaining NO drug for any other indication than the one specified is very costly and requires additional administrative actions. In the MICU, NO will be used in the following manner.

3.1.1 Support of Research Protocols:

NO will be used to support ongoing research through established protocols. Once a protocol is written and approved, the investigator will collaborate with INO Therapeutics (the sole provider of NO) to obtain approval for use of the drug. Once approval from INO Therapeutics is given, the drug and supplies will be dispensed to support the protocol at no charge. Current NO protocols utilize a facemask for the delivery of this drug.

3.1.2 Clinical Support of Inpatients:

NO may be used to support critically ill patients who present to the MICU with severe pulmonary hypertension due to acute respiratory failure. INO Therapeutics will provide the drug and supplies on a “Just in Time” basis. Charges will accumulate at \$3,000.00 for the first day, and \$125.00 each hour after the first 24 hours, with a cap of \$12,000.00 per patient. The Section Chief or his designee **must** be contacted to initiate this process.

4.0 INDICATIONS

- 4.1 To reduce pulmonary artery pressures due to pulmonary hypertension
- 4.2 To reduce pulmonary vascular resistance
- 4.3 To enhance oxygenation
- 4.4 As adjunctive therapy in treatment of ARDS

5.0 CONTRAINDICATIONS

5.1 Absolute contraindications:

- 5.1.1 Patients with congenital or acquired methemoglobinemia reductase deficiency

5.2 **Relative contraindications:**

- 5.2.1 Patients with a bleeding diathesis
- 5.2.2 Intracranial hemorrhage
- 5.2.3 Severe left ventricular failure

6.0 **HAZARDS/COMPLICATIONS**

- 6.1 Elevated methemoglobin levels
- 6.2 Nitrogen dioxide (NO₂) toxicity
- 6.3 Prolongation of PT/PTT
- 6.4 Increased left ventricular filling associated with rapid changes in pulmonary pressures
- 6.5 Rapid withdrawal of NO may result in rebound hypoxemia and pulmonary hypertension

7.0 **PRECAUTIONS**

- 7.1 When given via mechanical ventilator, an increase in exhaled tidal volumes might be noted. This increase occurs as a result of additional gas flow from NO into the circuitry. For example, at 40 ppm NO setting, the INOvent delivery system will add 10% more gas to that delivered to the ventilator and 5% more for 20 ppm setting.
- 7.2 Trigger sensitivity of the ventilator might be compromised, especially if the patient is on an assisted mode of ventilation.
- 7.3 The INOvent delivery system pulls gas from the breathing circuit via the gas sampling system at a flowrate of 230 ml/min. This may interfere with the patient's ability to trigger the ventilator if the patient is spontaneously breathing.
- 7.4 The set FiO₂ in the breathing circuit might be reduced with increases in the NO concentration (Refer to: Oxygen Dilution Chart" attached to this procedure).

8.0 ASSESSMENT OF NEED

- 8.1 Hypoxemia
- 8.2 Increased pulmonary artery pressures
- 8.3 Acute Respiratory Distress Syndrome
- 8.4 Acute chest syndrome or vaso-occlusive crises of sickle-cell anemia

9.0 ASSESSMENT OF OUTCOME

- 9.1 Improved oxygen saturation as measured by pulse oximetry
- 9.2 Increased arterial oxygenation
- 9.3 Reduced pulmonary artery pressures.

10.0 MONITORING DURING NITRIC OXIDE THERAPY

- 10.1 FiO_2
- 10.2 Tidal volume
- 10.3 Trigger sensitivity
- 10.4 Pulse oximetry
- 10.5 Arterial blood gases must be obtained at baseline and as follows:
 - 10.5.1 Post initiation
 - 10.5.2 Each hour or PRN as needed for six hours
 - 10.5.3 30 minutes after each NO concentration adjustment
 - 10.5.4 At any time when clinically indicated
- 10.6 Pulmonary artery pressure
- 10.7 Platelet count
- 10.8 NO_2 levels

11.0 FREQUENCY OF SYSTEM CHECKS

11.1 A ventilator INOvent system check should be done upon initiation of NO therapy. In addition to an initial check, the system should be checked:

11.1.1 Every two hours and PRN

11.1.2 Following any changes in ventilator and/or INOvent delivery system settings

11.1.3 Following an acute deterioration of the patient's condition as a result of decreasing or increasing NO concentration

12.0 EQUIPMENT

12.1 INOvent delivery system with two 800 ppm nitric oxide gas cylinders

12.2 Servo 300 ventilator

12.3 Pulse oximetry

12.4 Pulmonary artery catheter

12.5 Arterial line

12.6 Purge and performance setup

13.0 SET UP

13.1 Initial Connections

13.1.1 Connect regulator output hoses to the quick connect ports on the rear of the INOvent delivery system.

13.1.2 Connect regulators (hoses) to the NO therapy gas cylinders.

13.1.3 Confirm that the pressure in the NO gas cylinders is greater than 200 psi.

13.1.4 Connect the INOvent delivery system power cord to an electrical outlet. Ensure that the green power light is illuminated.

13.1.5 Connect the injector module to the electrical cable and injector tube. Connect the electrical cable and injector tube to the front panel of the unit.

- 13.1.6 Connect the sample line to the INOvent delivery system and, if necessary, empty the fluid bottle and/or change the filter.
- 13.1.7 Switch on the INOvent delivery system and wait for the start-up routine to complete. Confirm that both the buzzer and speaker sound.

13.2 Calibrations

The INOvent delivery system calibration function allows for low range calibrations of the NO, NO₂, O₂ sensors. This calibration can occur without taking the patient off the ventilator. The high range calibration is individually calibrated with special calibration gas.

WARNING: Ventilator changes should not be made while performing a low range calibration!

- 13.2.1 A **low range** calibration should be done initially and at least once per shift while in use. A low range calibration will zero the NO and NO₂ sensors and span the O₂ sensor to 21% (room air). Follow calibration procedures in Operator's Manual: Section 4-1 to 4-6.
- 13.2.2 A **high range** calibration should be done at least once per month using the calibration kit provided. The procedure requires that each sensor be calibrated individually. Separate cylinders of NO and NO₂ are required. A high range calibration of the O₂ cell can be performed using medical grade wall oxygen. Follow calibration procedures in Operator's Manual: Section 4-1 to 4-6.

14.0 PRE-USE PROCEDURES

NOTE: Prior to using the INOvent delivery system to administer NO to a patient, ensure that monthly maintenance procedures have been performed within the last 30 days.

These steps **MUST** be performed prior to placing a patient on the INOvent delivery system.

14.1 Initial Connections and Leak Test

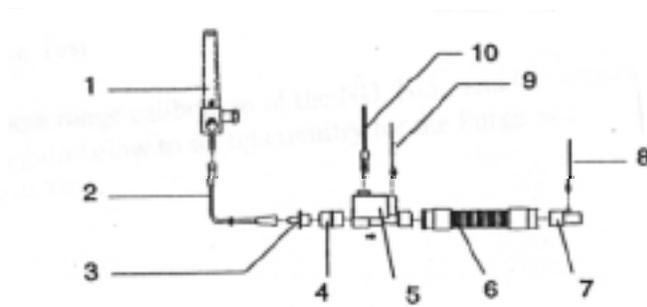
- 14.1.1 Connect the INOvent delivery system as described in the initial setup section.
- 14.1.2 Check cables and hoses for signs of wear or damage and replace as needed.

- 14.1.3 Switch the INOvent delivery system to ON and confirm that the buzzer and speaker sound. Wait for the start up routine to finish,
- 14.1.4 Turn each gas cylinder ON and confirm that there is at least 200 psig in each therapy gas cylinder.
- 14.1.5 Turn each cylinder valve off. Wait for 30 seconds and confirm that there is no decrease in the pressure reading on the regulator. Leave the cylinder valves off.

14.2 Purge and Performance Test

- 14.2.1 Perform a low range calibration of the NO, NO₂, and O₂ sensors.
- 14.2.2 Follow diagram below to set up circuitry for the Purge and Performance Test.

- 1 O2 Flowmeter
- 2 O2 Tubing
- 3 15M x 4.5 mm Adapter
- 4 22M/15F x 22M/15F Adapter
- 5 Injector Module
- 6 300 mm of 22mm hose
- 7 Sample Tee
- 8 Inspiratory Gas Sample Line
- 9 NO/NO₂ Injector Tube
- 10 Injector Module Electrical Cable



Circuit connections for purge and performance test

- 14.2.3 Ensure one end of the sample line is connected to the front on the INOvent delivery system and connect the other end to the sample tee as shown.
- 14.2.4 To purge the system, set the oxygen flow to 15 lpm and set the NO concentration to its maximum setting. Ensure that the regulator pressures fall to zero. When the NO therapy supply pressure gauges fall to zero, the INOvent delivery system has been purged.
- 14.2.5 Confirm that the "Low NO/NO₂ Pressure" and the "Delivery Failure" alarms sound to ensure the pressure has reached zero. This may take a few minutes depending on the NO supply gauges at the start of the test.
- 14.2.6 Once the alarms have sounded, turn on one NO cylinder. **DO NOT TURN ON THE OTHER CYLINDER.** The alarms will silence automatically.

14.2.7 Adjust the "SET NO" to 40 ppm, wait for 3 minutes or until the monitor readings are stable, and check that NO, NO₂, and O₂ readings, are within acceptable ranges. Acceptable ranges are listed below:

O₂ % v/v (± 3% v/v) = 95

NO₂ ppm max = 1.5

NO ppm (min/max) = 32/48

NOTE: *This table includes errors of the NO delivery system, the NO monitoring system, the calibration gas, and the NO therapy gas. If any of the monitor readings fall outside the ranges listed above, recalibrate the appropriate sensor.*

14.2.8 Adjust the "SET NO" concentration to zero.

14.2.9 Enter the "ALARM HISTORY" page and clear the screen of any resolved alarms.

14.3 Connecting the INOvent to the patient ventilator

14.3.1 Perform all pre use procedures.

14.3.2 Locate INOvent near the patient and ventilator.

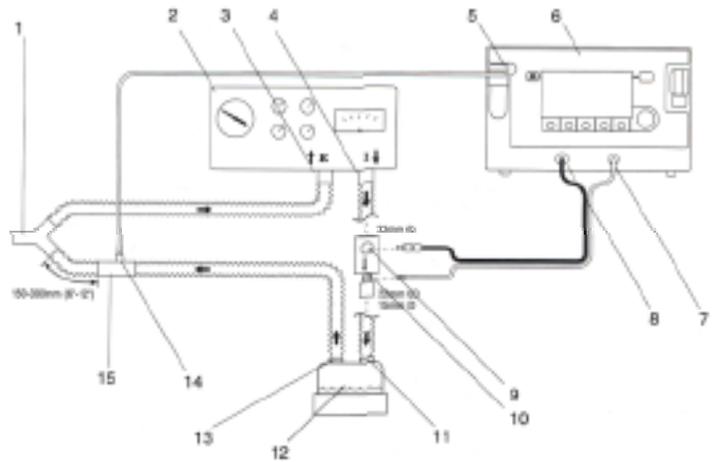
14.3.3 Connect the power cord to an emergency red outlet electrical supply.

WARNING: *If pre use procedures were performed more than 5 minutes prior to connecting to the patient's ventilator circuit, repeat the procedure to ensure that a high NO₂ is not delivered to the patient.*

14.3.4 Connect the injector module to the inspiratory limb of the breathing circuit between the inspiratory outlet of the ventilator and the inspiratory inlet of the humidification chamber.

14.3.5 Insert the sample tee into the inspiratory limb of the patient's breathing circuit approximately 6" to 12" away from the patient eye.

- 1 Patient wye
- 2 Ventilator
- 3 Ventilator Expiratory port
- 4 Ventilator Inspiratory post
- 5 Patient Gas sample line input connection
- 6 INOvent delivery system
- 7 NO/N2 Injector Tube front panel connection
- 8 Injector Module Cable front panel connection
- 9 Injector Module Electrical Cable connection
- 10 NO/N2 Injector Tube connection
- 11 Humidifier inlet
- 12 Humidifier
- 13 Humidifier outlet
- 14 Patient Gas sample line connection
- 15 Sample Tee



Typical System connection diagram (ICU ventilator)

15.0 INITIATE NO THERAPY

15.1 Set the delivered NO concentration to the desired level.

15.2 Set the measured inspired NO, NO₂, and O₂ measured alarm limit values.

16.0 MAINTENANCE OF THE INOvent SYSTEM

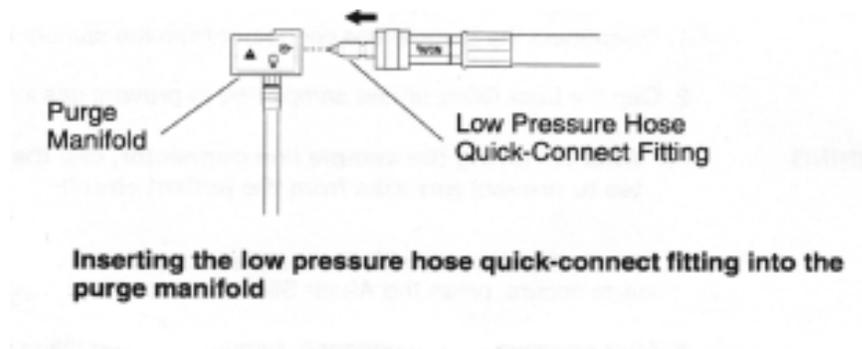
16.1 Changing NO Therapy Cylinders

16.1.1 The NO therapy gas cylinders should be changed whenever the cylinder pressure falls below 200 psig.

WARNING: *You must purge the regulator assembly immediately before using a new NO cylinder to make sure the patient continues to receive the correct NO concentration and does not receive high NO₂ concentrations.*

16.2 Purging the NO Therapy Cylinder

16.2.1 Use the purge manifold mounted on the cart located between the regulators in the back of the unit.



- 16.2.2 Determine which regulator assembly is not being used and requires purging.
- 16.2.3 On the regulator assembly that requires purging, disconnect the low pressure hose quick connect fitting from the NO, N₂ input on the rear of the INOvent delivery system.
- 16.2.4 Open the cylinder valve on the new NO therapy gas cylinder.
- 16.2.5 Close the cylinder valve on the new NO therapy gas cylinder.
- 16.2.6 Check for leaks at the cylinder valve outlet connection of the new cylinder with soapy water.
- 16.2.7 Insert the low pressure hose quick connect fitting into the purge manifold.
- 16.2.8 Firmly push and hold the quick connect fitting in place while the pressure falls to zero on the regulator gauge.
- 16.2.9 After the pressure drops to zero, reconnect the low pressure quick connect fitting to the NO/N₂ input on the rear of the INOvent delivery system.
- 16.2.10 Open the cylinder valve on the new cylinder.
- 16.2.11 Close the cylinder valve on the empty cylinder.
- 16.2.12 Replace the empty NO gas cylinder. Leave valve off.

17.0 ROUTINE AND SCHEDULED MAINTENANCE/INFECTION CONTROL

17.1 Between Patient Uses

- 17.1.1 Change sample line.
- 17.1.2 Clean the INOvent delivery system exterior surfaces with Dispatch.
- 17.1.3 Sterilize the injector module by steam autoclave.
- 17.1.4 Ensure the power cord is plugged into wall outlet to charge batteries at all times.

17.2 Daily (During Patient Use)

- 17.2.1 Ensure that NO therapy gas cylinder supply pressure is greater than 200 psig.
- 17.2.2 Perform low range calibration.
- 17.2.3 Empty the Fluid Trap Bottle.
 - 17.2.3.1 Empty the fluid trap bottle between patient uses or when bottle is half full.
- 17.2.4 Replace the Fluid Trap Filter Cartridge
 - 17.2.4.1 Replace the fluid trap filter cartridge between patient uses.

17.3 Monthly

- 17.3.1 A complete system checkout must be performed each month.

18.0 DOCUMENTATION STANDARDS

18.1 Calibration Data

- 18.1.1 The monthly calibration must be documented on the calibration sticker posted on top of the INOvent control box.
- 18.1.2 The low range calibration must be documented for each shift in the comments section on the "Continuous Ventilation Flow Record."
- 18.1.3 All patient information must be documented in the comments section of the "Continuous Ventilation Flow Record" according to CCT RCS documentation standards.

18.1.4 Documentation of NO delivery and status sheet must be completed.

19.0 REFERENCES

- 19.1 AARC Clinical Practice Guideline "Patient Ventilator System Checks."
- 19.2 CCMD :Care of Mechanically Ventilated Patient Standard of Practice."
- 19.3 James A. Bates, Department of Anesthesia, University of Iowa College of Medicine. "Inhaled Nitric Oxide: A selective pulmonary vasodilator."
- 19.4 B.H. Cuthbertson, P. Dellinger, O.L. Dyar, T.E. Evans, et al. UK guidelines for the use of inhaled nitric oxide therapy in adult ICUs. *Intensive Care Med* (1997) 23:1212-1218.
- 19.5 Luca M. Bigatello, William E, Hurford and Dean Hess. Use of inhaled nitric oxide for ARDS. *Respiratory Care Clinics of North America*. 3:3, September 1997; 1078-5337/97.
- 19.6 Ohmeda INOvent Delivery System for Nitric Oxide Therapy. Operation and Maintenance Manual.
- 19.7 Richard D. Branson, University of Cincinnati College of Medicine. Inhaled nitric oxide use in adults.

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