I. Purpose
Policy to provide guidelines for administration of nitric oxide gas to the neonatal population and to other select populations for the purpose of pulmonary vasodilation.

II. Policies
A. The terms nitric oxide and INOmax Delivery System will be used interchangeably throughout this document.
B. Nitric oxide (NO) is supplied as a blend of 0.8% nitric oxide and 99.2% nitrogen gas distributed under the name IKARIA.
C. The gas is supplied in concentrations of 100 ppm (parts per million) and 800 ppm.
D. Nitric Oxide is delivered to reduce pulmonary hypertension in neonates, thereby improving oxygenation.
E. Nitric Oxide is delivered to reduce the need for extracorporeal membrane oxygenation (ECMO) delivery in the pediatric population.
F. Nitric oxide delivery is indicated when all of the following criteria are met: the patient is a term or near-term birth neonate (> 34 weeks) up to 14 days of life; the patient is dependent on ventilatory support, adjunct therapy such as vasodilators, intravenous fluids, and bicarbonate therapy is administered as part of therapy, the patient has hypoxic respiratory failure associated with clinical or echocardiographic evidence of pulmonary hypertension.
G. A written physician’s order must be obtained to administer nitric oxide.
H. Documentation of therapy will be performed, at minimum, with each system change and each ventilator monitor.
I. Positive outcomes may be limited by, but not exclusive to the presence of collapsed alveoli, which indicates possible treatment with surfactant and high-frequency oscillatory ventilation.
J. The recommended dose of Nitric Oxide is 20 ppm; however, doses up to 80 ppm can be administered with caution.
K. Information about effectiveness in the age population above 14 days of life has not been studied.
L. Nitric oxide can be delivered with the INOmax delivery system only. Nitric Oxide will be delivered in the NICU, PICU, in adult ICUs or in the operating room.
M. Nitric oxide is to be administered via the Sechrist, VIP Bird, the Siemens 300 ventilator, HFOV (high frequency oscillating ventilator 3100A and 3100B).
N. “Neonate” is defined as a newborn infant up to 28 days of life.
SUBJECT: Nitric Oxide

O. Nitric oxide is contraindicated in the treatment of neonates known to be dependent on right-to-left shunt.

P. Methemoglobinemia, a byproduct of nitric oxide and oxyhemoglobin, increases significantly when Nitric Oxide is administered at doses >20 ppm. Methemoglobinemia levels >75 are usually treated by reducing the dosage of or discontinuing nitric oxide. This usually results in a return of the methemoglobinemia level to baseline over a period of hours.

Q. NO2 (nitrogen dioxide), a by-product of water, oxygen and nitric oxide, is harmful at elevated levels > 3 ppm and may cause acute lung injury. This is usually treated by reducing the dose of or discontinuing nitric oxide.

R. Abrupt discontinuation of nitric oxide may lead to worsening oxygenation and increasing pulmonary artery pressure.

S. Study evidence showed that adverse reactions of hypotension, withdrawal symptoms, atelectasis, hematuria, hyperglycemia, sepsis infection, stridor, and cellulitis occurred with an incidence of at least 5% more common in the nitric oxide group than in the placebo group.

T. The exposure limit set by the Occupational Safety and Health Administration for nitric oxide is 25 ppm, and for NO2, the limit is 5 ppm.

U. The maintenance company will clean and calibrate the delivery system after each patient use.

V. The use of Sildenafil Citrate tablet form for off-label use in specific patient populations should be explored before delivering nitric oxide gas.

III. Exceptional Therapy

A. Respiratory Care may approve the use of nitric oxide after an adequate evaluation by the pediatric intensive care attending and/or cardiovascular surgical attending physician has been performed.

B. Each patient undergoing nitric oxide utilization in the following circumstances will be reviewed retrospectively after use to ensure appropriateness of selection.

C. Any other use of nitric oxide will require an Institutional Review Board approved research protocol funded by a non-University source.

D. Criteria for exceptional therapy is selectively inclusive of:

1. The use of ventilatory support
2. The use of adjunct therapy such as vasodilators, intravenous fluids, and bicarbonate therapy
   AND
3. Pulmonary hypertension with reactive vascular beds in certain post-operative congenital heart defects such as:
   a. Atrioventricular Canal Defects
   b. Ventricular Septal Defects
   c. Total Anomalous Pulmonary Venous Connection
   d. Truncus Arteriosus
   e. Fontan, bi-directional Glenn and Norwood procedures
   f. Other rare congenital defects that show initial benefit from a trial of nitric oxide

4. Treatment of severe acute hypoxemic respiratory failure in the pediatric patient

5. Rare usage for the treatment of adult post-operative cardiac transplant or mitral valve or pulmonary embolectomy who show dramatic benefit from a trial of nitric oxide when all other medical interventions have failed. When possible, the use of nitric will be determined pre-operatively rather than intra-operatively.
IV. Procedure
A. Initiation of Therapy
The UMC institution agrees that when a patient is started on IKARIA TM Services and has reached a usage of 96 hours or greater we will notify the Provider by faxing a completed Expense Limitation form. Correspondence will continue with continuation of usage and will include dates.

B. Delivered Equipment
The provider will deliver to UMC the needed “88” size cylinders to keep at PAR levels as well as delivery systems for use and for standby. Weekly orders and deliveries are made after communication with customer service (877-566-9466). Either a coordinator or supervisor places weekly orders.

C. Continuation of Services
UMC contacts the provider via fax when continuation of therapy past 96 hours is needed. This information is filled out on a Expense Limitation Form provided by IKARIA.

D. Discontinuation of Services
UMC shall promptly notify the provider upon conclusion of each patient’s therapy that has completed greater than 96 hours of use. This communication is completed via faxed expense limitation form.

E. Equipment Damage and Repair
UMC shall not attempt to modify or repair any part of the INOvent delivery system but shall notify the Provider immediately. UMC shall not claim rights to any equipment or supplies provided as part of the INOtherapy Service. UMC will assume any and all losses or damage to the system components except that which is reasonably expected to result from normal usage in accordance with the instructions of the manufacturer. Accidental discharge of the cylinders is considered loss and damage to the component. UMC will provide protective storage of the system in this facility.

A. Procedure
a. System Calibration
Note: High calibration will be performed once a month. Documentation will be reflected on the flowsheet located on the top of the INOvent.
1. Check the cables and hoses for signs of wear or damage.
2. Turn the INOvent on and confirm that the buzzer and speaker alarms. Wait for the start-up routine to finish.
3. Confirm that your records indicate that a monthly system checkout has been done by verifying documentation kept on the top of the INOvent.
4. Perform a system high-pressure leak test.
5. With the INOvent ON, turn each cylinder valve ON the OFF. Check for adequate cylinder pressures. Wait for 30 seconds and check for any pressure decreases.
6. If there is any decrease, make sure that the auxiliary oxygen flowmeter to the manual NO system is turned off and checked for leaks around the hose connections using soapy water.
7. Check for leaks at the NO cylinder valve outlet connection using soapy water.

B. Low Calibration
Note: Low Calibration will be performed each shift. See the operator’s panel for instructions.
1. System Purge and Performance Test
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2. Manual NO Delivery System Purge and Performance Test
   a) Connect the manual NO delivery system.
   b) Disconnect the resuscitator bag.
   c) Connect the 22mm/15 mm sample tee (with the sample line connected) to the oxygen tubing using a 15m X 4.5 mm adapter.
   d) Set the oxygen flow at 15 LPM from the auxiliary flowmeter into the manual delivery system and make sure that float moved to the middle of the NO flow indicator window.
   e) Wait for the gas to flow through the oxygen tubing. Make sure the NO reading is 20+8 ppm and the NO2 reading is <1.0 ppm. If the NO2 reading is >1.0, continue flowing gas until the limit is reached.
   f) Reduce the O2 flow to 1 LPM and make sure that the float drops to the bottom of the NO flow indicator.
   g) Set the O2 flow to zero and disconnect the sample tee and 15 M X 4.5 mm adapter from the oxygen tubing.
   h) Reconnect the resuscitator bag to the oxygen tubing.

3. Ventilator Set-up for Delivery of Nitric Oxide
   a) Perform the preclinical procedures.
   b) Place the injector module before the humidifier with the arrow pointed in the direction of the gas flow.
   c) Place the sampling tee piece inline on the inspiratory limb of the circuit proximal to the patient.
   d) Set NO delivery to the desired setting.
   e) Check the oxygen reading on the INOvent. Compensate for any decrease in FI02 by decreasing oxygen delivery to achieve your FI02 goal. The FI02 is diluted by the introduction of NO into the ventilator circuit.
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f) Compensate for any tidal volume loss if a volume ventilation mode is used by increasing the tidal volume to the ordered value. The sampling line withdraws 230 mL per minute. Divide 230 mL by breaths per minute; the product equals the volume loss per breath.

g) Record NO, NO2 and O2 on the appropriate records when any ventilator check is performed.

VI. References
A. AARC Clinical Practice Guidelines, 1999
B. Correspondence of Bobby J. Heat, MD April 27, 2000
C. Professor of Surgery; Chief, Cardiothoracic Surgery
D. Program Director/Thoracic Surgery
E. Correspondence of Thomas A. Walker, MD, May 1, 2000
F. Assistant Professor of Pediatrics; Division of Pediatric Critical Care
G. InOmax Information Sheet, January 2000
H. Inomax Delivery system Operator’s Manual
I. INOTHERapeutics, Contract Agreement, March 15, 2000
J. Taber’s Cyclopedic Medical Dictionary