Guideline Title: Nitric Oxide (NO)

Summary: Nitric oxide is administered as an inhaled gas and produces selective vasodilatation of the pulmonary arterioles without systemic effect due to its short half life. Delivery of Nitric Oxide is by the INOmax DS IR system.

Approved by: ICU Director A/ Prof Michael Parr

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Replaces Existing Guideline: New Guideline

Contents:
1. Background Information
2. Definitions
3. Introduction
4. Policy Statement
5. Policy/Guidelines
   A. Actions
   B. Indications
   C. Contraindications
   D. Side effects
   E. Dosage
   F. Precautions
   G. Complications
   H. Equipment
   I. Set up
   J. Pre use procedures
   K. Connection
   L. Maintenance
   M. Monitoring
   N. Transporting
   O. Discontinuation of therapy
   P. Alarms
6. Clinical Issues
7. Performance Measures
8. References

1. Background Information: Nitric oxide (NO) is a gas molecule with selective vasodilatation properties. NO is the active metabolite of a number of other vasodilators, including sodium nitroprusside and nitroglycerin. 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 haemoglobin. The by-product of this reaction produces increased levels of methaemoglobin. Methaemoglobin will not carry oxygen, and therefore, its level must be closely monitored during NO therapy. Half-life –, inhaled NO has an effective half-life of 15 to 30 seconds at a dose of 5 to 80 ppm.
Nitric oxide is delivered to the patient by mechanical ventilation after dilution with an oxygen/air mixture using the INOMaxDSIR.

There are two ways to deliver nitric oxide, either continuously or by intermittent flow. The gold standard for nitric oxide delivery is a controlled inspiratory injection via the inspiratory limb which decreases the bolus effects seen with continuous systems.

**INOBLENDER**
The INOBLENDER allows users to select a concentration of INOMAX, (nitric oxide in a balance of nitrogen), to be mixed into a user set flow of oxygen which is delivered to patient. The intended use for the INOBLENDER is as a back up to a primary INOMAX delivery system; or for short term attended use when a primary delivery device cannot practicably be used.

2. **Definitions/ Abbreviations**¹¹,¹²

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>N₂</td>
<td>Nitrogen</td>
</tr>
<tr>
<td>NO</td>
<td>INOMax (nitric oxide) for inhalation</td>
</tr>
<tr>
<td>NO₂</td>
<td>Nitrogen dioxide</td>
</tr>
<tr>
<td>NO/N₂</td>
<td>Nitric oxide (NO) and (N₂) gas mixture</td>
</tr>
<tr>
<td>O₂</td>
<td>Oxygen</td>
</tr>
<tr>
<td>ppm</td>
<td>Parts per million</td>
</tr>
<tr>
<td>Set NO</td>
<td>The dose of INOMax set by the user</td>
</tr>
<tr>
<td>v/v</td>
<td>Volume to volume</td>
</tr>
</tbody>
</table>

3. **Introduction:**
   The risk addressed by this policy:

   **Patient Safety**

   The Aims / Expected Outcome of this policy:

   Staff caring for patients who require NO will have the knowledge and skills to provide safe and effect care of the patient and the INOMax system
4. Policy Statement:

- All care provided within Liverpool Hospital will be in accordance with infection prevention/control, manual handling and minimisation and management of aggression guidelines.
- Inhalation of nitric oxide via the INOmax Delivery System will be performed in ICU by personnel trained and competent in this procedure.
- The handover circuit checklist must be attended on handover every shift.
- Methaemoglobin level must be closely monitored during NO therapy.
- WARNING: Ventilator changes should not be made while performing a low range calibration.
- NOTE: Prior to using the INOmax delivery system to administer NO to a patient, ensure that monthly maintenance procedures have been performed within the last 30 days. Log with Equipment Officers.
- The INOmax DSIR transceiver is located under the cart cover and should be protected from outside IR sources. If there is interference and/or High frequency and/or high intensity light emission with the INOmax DSIR/INO metre communication, the cylinder icon on the user screen will not be displayed and a "Cylinder Not Detected" alarm will activate. DO NOT place anything on top of the cylinder.
- Laerdal bag should be functioning, set up and attached to O₂ outlet on the INOblender at all times in case of NO delivery failure.
- Before connecting to patient the laerdal bag must be squeezed 3-4 times to eliminate the nitric that has been sitting in the bag.

- The valve cylinder must be turned off when treatment is completed.
- When attaching the injector module to the humidifier the injector must be placed in with humidifier attachment and the arrow pointing down.

- Pre use checkout/procedures MUST be performed prior to placing a patient on the INOMax delivery system.
- The purge procedure must be followed to help ensure NO₂ is purged from the system before the manual resuscitator bag is connected to the patient.
- Do not use pneumatically powered nebulizers with the INOblender. This will result in significant over delivery of INOMAX in excess of 80 parts per million (ppm).
- When not in use, the oxygen flow metre and the INOMAX cylinder valve should be turned off.
- The inspired INOMax concentration must be measured continuously in the inspiratory limb of the circuit near the patient.
- For patient safety, appropriate alarms must be set for INOMax (± 2 ppm of the prescribed dose), NO₂ (1 ppm), and FiO₂ (± 0.05).
- The INOMax gas cylinder pressure must be displayed to allow timely gas cylinder replacement without inadvertent loss of therapy and backup gas cylinders must be available to provide timely replacement.
- INOMax therapy must not be ceased for manual ventilation, suctioning, patient transport, and resuscitation.
- In the event of a system failure or a wall-outlet power failure, a backup battery power supply (blue power point) and reserve nitric oxide delivery system must be available. The power supply for the monitoring equipment should be independent of the delivery device function.
• When the backup NO delivery mode is used, a flow of at least 5.0 L/min should be present in the ventilator circuit to avoid INOMAX concentrations greater than 40 ppm.

5. Principles / Guidelines

A. Actions
- Is a gas for inhalation that contains nitric oxide diluted in nitrogen gas at 400 or 800 parts per million (ppm)
- When nitric oxide is administered as an inhaled gas it produces selective vasodilatation of the pulmonary arterioles without systemic effect due to its short half life.
- Vasodilatation of the pulmonary arterioles optimises gas exchange by opening up the pulmonary vasculature, allowing uptake of oxygen and removal of carbon dioxide from the blood as it flows through the lungs.
- Nitric appears to increase the partial pressure of arterial oxygen (PaO2) by dilating pulmonary vessels in better ventilated areas of the lung, redistributing pulmonary blood flow away from lung regions with low ventilation/perfusion (V/Q) ratios toward regions with normal ratios. It can therefore improve oxygenation in ARDS.
- Cardiac function is also improved as the reduction in pulmonary artery pressure reduces the stress on the right ventricle.

B. Indications
- ARDS
- Pulmonary hypertension
- Post-cardiac surgery (pulmonary hypertension)
- Cardiac transplantation
- Weaning off ECMO

C. Absolute contraindications
- Patients with congenital or acquired methaemoglobinemia reductase deficiency

Relative contraindications
- Patients with a bleeding diathesis
- Intracranial hemorrhage
- Severe left ventricular failure

D. Side effects

Common
- thrombocytopenia
- hypokalaemia
- hypotension
- atelectasis
- hyperbilirubinaemia

Uncommon
- Increase in methaemoglobin, causing reduced oxygen carrying capacity.

May be seen but the frequency is not known
- Bradycardia
- Oxygen desaturation/hypoxemia due to sudden withdrawal of the treatment
- Headaches, dizziness, dry throat or shortness of breath following accidental ambient air exposure to nitric oxide (e.g. leakage from equipment or cylinder).

Environmental exposure for staff
Inhaled nitric oxide therapy at doses up to 20 ppm does not appear to pose a risk of excessive occupational exposure to nitric oxide or nitrogen dioxide to health care workers during routine delivery of critical care.
E. Dosage and administration ², ¹³:(See flowchart next page)

**Adult Respiratory Distress Syndrome (ARDS)**
- Inhaled nitric oxide is a Schedule 4 drug and must be prescribed by medical Officer
- The maximum recommended dose of INOmax is 20ppm
- Nitric oxide should be reserved for those patients who are optimally ventilated, with optimal PEEP, inverse ratio ventilation and prone positioning as appropriate
- Maximum improvement in oxygenation occurs in most patients at 20 ppm or less; rarely 40 ppm is required
- After 4-24 hours of therapy the dose should be weaned to 5 ppm provided that PaO₂ is adequate at the lower dose

**Weaning (ARDS) ¹³**
*Slow weaning is advised over hours to days to avoid vasoconstriction and rebound deterioration in oxygenation*

**Weaning Protocol:**
- PaO₂ > 63mmhg on
- 40% O₂ or less with
- PEEP 8cmH₂O or less
- Inhaled nitric oxide reduced by 20% every 30 minutes as long as threshold is maintained or
- 1 ppm for 30 minutes to 1 hour
- If threshold not maintained nitric oxide returned to the previous level and weaning attempt in another 12 hrs

**Pulmonary Hypertension**
- Commence with 5-6ppm
- Increase to max 20ppm according to ABG and PAP
Dosage and administration Flow chart:\(^2,^{13}\):

Consultant writes prescription for Nitric oxide (NO) Therapy

Document baseline observations for
PaO\(_2\), SpO\(_2\), MAP, PAP, CI, PVR

Start Nitric Therapy at 20ppm

After 15-30 mins is there an increase in
PaO\(_2\), SpO\(_2\), MAP, PAP, CI, PVR

No

Increase NO to 40ppm

Cease NO

Yes

Wean NO to 10ppm

After 15-30 mins is there an increase in
PaO\(_2\), SpO\(_2\), MAP, PAP, CI, PVR

No

Return NO to 20ppm
Evaluate for weaning every 4 hrs

After 15-30 mins is there an increase in
PaO\(_2\), SpO\(_2\), MAP, PAP, CI, PVR

Yes

Wean NO to 5ppm

Yes

Leave at 5ppm
Evaluate to cease every 4 hrs

No

Return NO to 10ppm
Evaluate for weaning every 4 hrs

After 15-30 mins is there an increase in
PaO\(_2\), SpO\(_2\), MAP, PAP, CI, PVR

Yes

Wean NO to 10ppm

No

Return NO to 30ppm
Evaluate for weaning every 4 hrs

After 15-30 mins is there an increase in
PaO\(_2\), SpO\(_2\), MAP, PAP, CI, PVR

No

Return NO to 20ppm
Evaluate for weaning every 4 hrs

After 15-30 mins is there an increase in
PaO\(_2\), SpO\(_2\), MAP, PAP, CI, PVR

Yes

Wean NO to 10ppm

No

Return to 30ppm
Evaluate for weaning every 4 hrs

After 15-30 mins is there an increase in
PaO\(_2\), SpO\(_2\), MAP, PAP, CI, PVR

Yes

Wean NO to 10ppm

No

Return to 40ppm
Evaluate for weaning every 4 hrs

After 15-30 mins is there an increase in
PaO\(_2\), SpO\(_2\), MAP, PAP, CI, PVR
F. Precautions

- 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 INOmax delivery system will add 10% more gas to that delivered to the ventilator and 5% more for 20 ppm setting. The net result of the of the INOmax DS\text{IR} on the delivered minute volume can be calculated as follows:

\[
\text{Additional INOMAX volume added per minute} = \frac{\text{INOMAX dose} \times \text{Minute Volume}}{\text{Cylinder Concentration} - \text{INOMAX Dose}}
\]

For a dose of 20 ppm the additional volume would be
\[
\frac{20 \times 10}{800 - 20} = 0.25 \text{ L/min}
\]

To calculate the net change in minute volume:
\[
0.25 \text{ L/min INOMAX added} - 0.23 \text{ L/min removed (sample system)} = 0.02 \text{ L/min (net change)}
\]

- Trigger sensitivity of the ventilator might be compromised, especially if the patient is on an assisted mode of ventilation. The INOMax delivery system pulls gas from the breathing circuit via the gas sampling system at a flow rate of 230 ml/min. This may interfere with the patient's ability to trigger the ventilator if the patient is spontaneously breathing. Trigger sensitivity should not be set lower than 1L/min
- The set FiO2 in the breathing circuit might be reduced with increases in the NO concentration

### Oxygen Dilution Chart

For delivery with 800 ppm cylinder of INOMAX\textsuperscript{®} (nitric oxide) for inhalation (Illustrative Only)

<table>
<thead>
<tr>
<th>INOMAX Dose (ppm)</th>
<th>.21</th>
<th>.40</th>
<th>.60</th>
<th>.80</th>
<th>1.00</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>0.21</td>
<td>0.40</td>
<td>0.59</td>
<td>0.79</td>
<td>0.99</td>
</tr>
<tr>
<td>20</td>
<td>0.20</td>
<td>0.39</td>
<td>0.59</td>
<td>0.78</td>
<td>0.98</td>
</tr>
<tr>
<td>40</td>
<td>0.20</td>
<td>0.38</td>
<td>0.57</td>
<td>0.76</td>
<td>0.95</td>
</tr>
<tr>
<td>80</td>
<td>0.19</td>
<td>0.36</td>
<td>0.54</td>
<td>0.72</td>
<td>0.90</td>
</tr>
</tbody>
</table>

\(\Delta\) Caution FiO2 less than 21%

Please note: The calculations on this chart have been determined based on an 800 ppm cylinder of INOMAX (nitric oxide) for Inhalation.

This chart is representative of a range of doses available on the INOmax DS\text{IR} and doses higher than 20 ppm are not the recommended therapeutic dose.
G. Complications/ hazards

- Elevated methaemoglobin levels
- Nitrogen dioxide (NO2) toxicity
- Prolongation of PT and APTT
- Increased left ventricular filling associated with rapid changes in pulmonary pressures
- Rapid withdrawal of NO may result in rebound hypoxemia and pulmonary hypertension

Overdose

- Overdose of nitric oxide results in elevations in methaemoglobin and NO2.
- Elevated NO2 may cause acute lung injury.
- Elevations in methaemoglobinemia reduce the oxygen delivery capacity of the circulation. In clinical studies, NO2 levels > 3 ppm or methaemoglobin levels > 7% were treated by reducing the dose of, or discontinuing, INOmax.
- Methaemoglobinemia that does not resolve after reduction or discontinuation of therapy can be treated with intravenous vitamin C, intravenous methylene blue, or blood transfusion, based upon the clinical situation

H. Equipment

- INOmax delivery system with two 800ppm Nitric Oxide gas cylinders
- Drager Ventilator
- Pulse oximetry
- Pulmonary artery catheter
- Arterial blood pressure monitoring

For Purge and performance setup:
- Injector module
- Sampling line
- Tee adaptor
- Straight adaptor
- Grey adaptor (nose)
- Blue corrugated tubing
- Injector module cable
- Injector module tubing
- Oxygen tubing

- Water trap cartridge
- Connector (humidifier attachment)
I. **G. Setup**\(^6,11\)

**Initial Connections**
- Inspect regulator for signs of damage
- Connect regulator to NO gas cylinder
- Connect regulator output hoses to the quick connect ports on the rear of the INOmax delivery system

- Prior to connecting a regulator hose, ensure the inlet connectors, on the INOmax DSIR unit, have the knurled sleeve set in the back position (toward the INOmax DSIR unit). Should the sleeve be in the forward position the inlet valve will be open and the INOMAX regulator hose will not securely connect to the inlet
- Insert the connector from the regulator hose into the gas inlet. Ensure the knurled sleeve moves and clicks into the forward position, locking the connector in place.
- To disconnect the INOmax DSIR regulator hose, push the knurled sleeve toward the back of the INOmax DSIR unit until the hose disengages

- Connect the INOblender with the INOmax DSIR. Connect the INOblender inlet hose to the INOmax blender outlet and slide the Quick-Connect cover into place.
- Connect oxygen supply (wall source or cylinder oxygen) hose to \(O_2\) inlet fitting on back of INOblender.
- Connect the Infrared cable from the INOmax DSIR cart to the back of the INOmax

- Connect the INOmax delivery system power cord to an electrical outlet.
- Ensure that the green power light is illuminated
- Turn the INOmax DSIR ON and wait for the start-up routine to complete. Confirm that both the buzzer and speaker sound.
- Ensure water trap bottle and water separator cartridge are in place.

- Connecting the cables and injector module (see instructions in diagram below)

- INOmax is now ready for Pre use checkout procedures (see next page)
J. Pre use procedures

Follow CHECKOUT CARD below

**INOMax DSIR® Pre-Use Procedure**

**Initial Connections:**
- Check grey INOblander hose, black infrared cable and oxygen supply is connected
- Ensure water trap and water separation cartridge are in place
- Turn ON INOMax DSIR
- Check white plastic tip on regulator for damage
- Connect high pressure regulator to INOMax cylinder and INOMax DSIR

**Step 1. Perform high pressure leak test**

**Note:** Make sure INOMax cylinder icon is present and INOMax DSIR backup and INOblander are OFF

- Open/Close INOMax cylinder valve
- Wait 30 seconds and ensure no pressure drop

**Step 2. Perform low range calibration (may take 2-3 minutes)**

**Note:** Once the calibration is completed (bars turn green), press the menu button twice to return to the main screen

**Step 3. Perform purge and alarm verification**

Assemble connectors and tubing as shown.
Connect purge circuit to DSIR

- O2 tubing
- 15M X 4.5mm adaptor
- 22M/15F X 22M/15F adaptor
- Injector module
- Grey Injector module electrical cable
- NO injector tubing line
- Alligence paediatric extension
- Gas sample tee
- Patient gas sample line

- a. Ensure INOMax cylinder valve is closed
- b. Connect to wall or cylinder oxygen
- c. Set O2 Flowmeter to 10 L/min
- d. Set the INOMax dose to 40 ppm for 800 ppm cylinders. (A 'Cylinder Valve Closed' alarm will occur)
- e. Purge is complete when 'Low NO/N2 Pressure' alarm activates
- f. Open cylinder valve
- g. Turn INOMax close to zero
  
  **Note:** The 'Set Dose is Zero, Close Cylinder Valve' indicator will appear, at this point do not close the cylinder valve

**Important:** This quick reference guide is provided for general information only and is not a substitute for the INOMax DSIR & INOblander Operation and Maintenance Manuals. Refer to these manuals for detailed information and applicable cautions & warnings.

www.ikariaaust.com  24/7 Customer Care and Technical Support 1300 198 565
Step 4. Perform backup delivery test

a. Ensure oxygen flow of 10 L/min
b. Turn Backup delivery ON

c. Verify ‘Backup ON’ alarm activates

d. Verify values

<table>
<thead>
<tr>
<th>No Cylinder</th>
<th>NO (ppm)</th>
<th>NO₂ (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>800 ppm</td>
<td>14-26</td>
<td>≤ 1.0</td>
</tr>
</tbody>
</table>

e. Turn Backup delivery OFF

Step 5. Complete INOmax DS_{IN} performance test

a. Ensure oxygen flow of 10 L/min
b. Set INOmax dose to 40 ppm for 800 ppm cylinders and allow values to stabilize
c. Verify values

<table>
<thead>
<tr>
<th>Set INOmax Dose</th>
<th>40 ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acceptable NO Values</td>
<td>35-45 ppm</td>
</tr>
<tr>
<td>Acceptable NO₂ Values</td>
<td>&lt; 1.5 ppm</td>
</tr>
<tr>
<td>FIO₂ Values</td>
<td>95% ± 3%</td>
</tr>
</tbody>
</table>

d. Turn the INOmax dose to zero

Step 6. Perform INOblender test

a. Remove the Pre-Use set-up oxygen tubing from the oxygen flowmeter and connect it to the front of the INOblender
b. Remove the injector module from the Pre-Use set up and reconnect the adapters
c. On the INOblender - Set the INOmax dose to 40ppm and O₂ flow to 10 L/min
d. Verify values on the INOmax DS_{IN}

<table>
<thead>
<tr>
<th>Cylinder Concentration</th>
<th>Acceptable NO Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>800 ppm Cylinder</td>
<td>32 - 48 ppm</td>
</tr>
</tbody>
</table>

e. Turn the dose and flow to zero and remove the Pre-Use set-up from the INOblender
f. If starting therapy within 10 minutes, the INOmax DS_{IN} is now ready to connect to the patient

WARNING: If starting therapy is delayed for more than 10 minutes, the INOmax DS_{IN} is now ready to connect to the patient.

Step 7. To Depressurize

a. Close INOmax cylinder valve
b. Purge the pressure from the regulator using the purge port on the back on the INOmax DS_{IN}
c. Reconnect regulator line to INOmax DS_{IN} inlet

WARNING: If the INOmax DS_{IN} is depressurised and not used within 12 hours, repeat Pre-Use Procedure
Depressurise /purging the regulator flow line

- If not immediately connecting to a patient, turn the INOMAX cylinder to OFF

- Purge the pressure from the regulator using the purge port on the back of the INOmax DSIR

- Reconnect regulator line to INOmax DSIR inlet

If the INOmax DSIR is depressurized and not used within 12 hours, repeat pre-use procedure

K. Connecting the INOmax to the patient ventilator

- Perform all pre use procedures.
- Locate INOmax near the patient and ventilator.
- 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.

- Connect the adaptor for humidifier to injector module

- 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.
The arrow on the injector module must be pointing down.

- Make sure the port in the sample tee is pointing upward (this helps to avoid fluid accumulation in the sample line).
- The distance between the sample tee and the patient wye should be between 150 to 300 mm (6-12 inches) long. Important: This will minimize the sampling of mixed inspired / expired concentrations and to ensure correct patient INOMAX®/NO2 measurement.
Initiating NO therapy

- Set the delivered NO concentration as per administration guidelines (see page 7)
- Any benefit from inhaled nitric oxide administration occurs within 5-30 minutes
- Set the measured inspired NO, NO2, and O2 measured alarm limit values.

L. Monitoring during Nitric Oxide therapy

- **PaO2**
  - Monitor with ABG
  - Obtain baseline pre initiation of therapy
  - hourly for 6 hours
  - 30 minutes after each NO concentration adjustment
  - Maintain PaO2 greater than 80mmHg

- **Methaemoglobin (MetHb)** should remain less than 3-5%
  - levels to be checked on ABG prior to commencement
  - then hourly until NO reduced to stable level then 12hrly
  - MetHb levels of 1.6% or greater must be reported to Medical staff
  - if MetHb worsens monitor until <5%
  - . If the fraction of methaemoglobin rises above 5% that potentially compromises adequate oxygen delivery, the INOmax dose should be decreased and the administration of reducing medicinal products such as methylene blue may be considered

- **Tidal volume**
  - When using volume ventilation with the INOmax DSIR, the measured tidal volume delivered to the patient shows small changes depending on the NO setting being used due to the addition and subtraction of gases by the delivery system. Some minor ventilator adjustments to the minute volume may be required

- **Trigger sensitivity**
  - The addition and subtraction of gases by the INOmax DSIR may affect the trigger sensitivity of the ventilator when using synchronized modes of ventilation. This may cause the ventilator to auto-trigger in ventilators which have flow trigger modes, especially where the trigger flow is set to less than 1 L/min. The trigger sensitivity of the ventilator should be checked after connecting the INOmax DSIR delivery system.

- **Pulse oximetry**
  - Greater than 94%

- **Calcium, Platelet and APPT daily**

- **Nitrogen Dioxide (NO2) levels**
  - Occupational health and Safety Administration guidelines limit NO2 exposure to 5 ppm continuous exposure over 8 hours

- **Monitoring the environment (once a day)**

Ikaria. INOmaxDSIR Operation and maintenance manual 2013
M. MAINTENANCE OF THE INOmax SYSTEM

1. Changing NO Therapy Cylinders
   - The NO therapy gas cylinders should be changed whenever the cylinder pressure falls below 200 psi.
   
   **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.

   **Purging the NO Therapy Cylinder**
   - Use the purge manifold mounted on the cart located between the regulators in the back of the unit.
   - Determine which regulator assembly is not being used and requires purging.
   - 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.
   - Open the cylinder valve on the new NO therapy gas cylinder.
   - Close the cylinder valve on the new NO therapy gas cylinder.
   - Check for leaks at the cylinder valve outlet connection of the new cylinder with soapy water.
   - Insert the low pressure hose quick connect fitting into the purge manifold.

   - Firmly push and hold the quick connect fitting in place while the pressure falls to zero on the regulator gauge.
   - 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.

   - Open the cylinder valve on the new cylinder.
   - this may activate the “Two Cylinders Open” alarm until the empty cylinder valve is closed

   - Close the cylinder valve on the empty cylinder.
   - Replace the empty NO gas cylinder. Leave valve off.
ii. **Routine and scheduled maintenance/infection control**

*Between Patient Uses*
- Change sample line.
- Clean the INOvent delivery system exterior surfaces
- Sterilize the injector module by steam autoclave.
- Ensure the power cord is plugged into wall outlet to charge batteries at all times.

*Daily (During Patient Use)*
- Ensure that NO therapy gas cylinder supply pressure is greater than 200 psi.
- Perform low range calibration.
- Empty the Fluid Trap Bottle.
- Empty the fluid trap bottle between patient uses or when bottle is half full

**Water trap**
- Empty the water trap bottle routinely. Allowing it to fill and overflow may cause system errors.
- A “Water Bottle Full” message will remind you to empty and clean the fluid trap should it become full

- Remove the bottle by pulling it straight down
- Discard the contents according to an approved fluid waste disposal policy.
- Clean the bottle.
- Replace the bottle by pushing it up into position.
- Check for leaks by running the system and occluding the sample line until the sample line occlusion alarm message appears
- Replace the Fluid Trap Filter Cartridge
- Replace the fluid trap filter cartridge between patient uses.

*Monthly*
- A complete system checkout must be performed each month.
N. Transporting

Warning: Loss of communication between the INOmax DSIR and the INOMAX cylinder for more than one hour will result in interruption of INOMAX delivery.

1. Connect a high pressure regulator to an INOMAX cylinder and tighten the fitting to the INOMAX cylinder
2. Connect the INOMAX regulator hose to one of the INOMAX inlets on the back of the INOmax DSIR

3. Connect the infrared cable from the Transport Regulator/Cap Assembly to the back of the INOMax DSIR. The connector clicks to indicate that it is latched in place.

4. Place the Cap Assembly over the INOmeter. Be sure to align the keyway inside the Cap Assembly with the iButton on the INOmeter

5. Grasp the Cap Assembly to open cylinder valve
O. Discontinuation of therapy \(^6, 11\) (see administration flowchart page 7)

- The INOmax dose should not be discontinued abruptly as it may result in an increase in pulmonary artery pressure (PAP) and/or worsening of blood oxygenation (PaO2).
- Weaning from inhaled nitric oxide should be performed with caution.
- For patients transported to other facilities for additional treatment, who need to continue with inhaled nitric oxide, arrangements should be made to ensure the continuous supply of inhaled nitric oxide during transportation.
- There should be access at the bedside to a reserve nitric oxide delivery system.
- Abrupt discontinuation of NO can precipitate rapid worsening of ventilation-perfusion matching and/or pulmonary hypertension, which typically manifests as hypoxemia and/or hemodynamic compromise.

P. Alarms / Troubleshooting \(^11\) SEE APPENDIX 2 FOR DETAILED ALARMS

Backup NO Delivery
- The backup is intended for short term use when the electronic delivery system fails until a replacement NO delivery device can be brought to the bedside.
- The backup delivery is activated through the backup switch on the front panel. The INOMAX dose should then be turned off.
- The backup mode delivers a variable concentration of NO to the patient depending on the ventilator flow being used.
- If the display is active, the main screen indicates that backup delivery is on and the set dose is turned off.
- When the backup NO delivery mode is used, a flow of at least 5 L/min should be present in the ventilator circuit to avoid INOMAX concentrations greater than 40 ppm.
- The table below indicates the nominal concentrations delivered for different ventilator gas flows.

<table>
<thead>
<tr>
<th>Ventilator/Gas Flow (L/min)</th>
<th>5</th>
<th>7.5</th>
<th>10</th>
<th>15</th>
<th>20</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO Concentration (ppm)</td>
<td>40</td>
<td>27</td>
<td>20</td>
<td>13</td>
<td>10</td>
</tr>
</tbody>
</table>

INOMAX cylinder conc. X 0.25 L/min / ventilator flow = delivered dose

- Advantage of this backup delivery is the patient does not have to be removed from ventilator (e.g. ARDS patient)

INOBLENDER
- The intended use for the INOblender is as a back up to a primary INOMAX delivery system; or for short term attended use when a primary delivery device cannot practicably be used.
- The INOblender allows users to select a concentration of INOMAX, (nitric oxide in a balance of nitrogen), to be mixed into a user set flow of oxygen which is delivered to patient.
- Because of the potential for inhalation of excessive concentrations of NO2, and the difficulty in monitoring the peak inhaled NO2 concentrations, ventilation with a hyperinflation bag or self inflating bag is intended only for short term use.
- To minimize the delivered concentration of NO2, the following steps should be taken for use with the manual resuscitator bags:
  - Concentrations greater than 20 ppm NO should not be used because of excessive NO2 generation.
  - Use the smallest bag adequate to deliver the desired tidal volume.
  - Inspiratory tubing lengths greater than 72 inches should not be used.
  - Use the highest fresh gas flow rate (up to 15 L/min) that is practical.
  - Use the lowest practical inspired oxygen concentration.
After starting fresh gas flow, squeeze the bag several times to empty residual gas in the bag prior to using the system to ventilate a patient.

6. Clinical Issues\textsuperscript{5,6}:

- The handover circuit checklist must be attended on hand over every shift (see appendix 1)

Special precautions for storage\textsuperscript{11}

- All regulations concerning handling of pressure vessels must be followed.
- Store gas cylinders indoors in well-ventilated rooms or outdoors in ventilated sheds where they are protected from rain and direct sunlight.
- Protect the gas cylinders from shocks, falls, oxidising and flammable materials, moisture, and sources of heat or ignition.
- Storage in the pharmacy department
- The gas cylinders should be stored in an airy, clean and locked place, for storage of medicinal gas only. Inside this place, a separate premise should be dedicated to the storage of nitric oxide gas cylinders
- Empty gas cylinders will be collected by the supplier.

7. Performance Measures

All incidents are documented using the hospital electronic reporting system: IIMS and managed appropriately by the NUM and staff as directed.

8. References / Links

2. Product Information. INOmax.2007
4. Nitric Oxide: Drug Information. uptodate.com 2014
7. Exposure of intensive care unit nurses to nitric oxide and nitrogen dioxide during therapeutic use of inhaled nitric oxide in adults with acute respiratory distress syndrome.
10. Bench-to-bedside review: Inhaled nitric oxide therapy in adults
12. Inhaled nitric oxide in adults with pulmonary hypertension. Darren B Taichman, MD, PhD. Uptodate 2014
13. Ikaria. INOmaxDS\textsubscript{IR}. Operation and maintenance manual 2013
Author: ICU CNE (P. Nekic)
Reviewers: ICU – CNC, CNEs, NM, NUMs, Staff Specialists, CNSs
Endorsed by: Prof M. Parr, Medical Director ICU.
## 9. Appendix 1
### HANDOVER CHECKLIST

<table>
<thead>
<tr>
<th>NITRIC THERAPY HANDOVER CHECKLIST</th>
<th>MON</th>
<th>TUES</th>
<th>WED</th>
<th>THU</th>
<th>FRI</th>
<th>SAT</th>
<th>SUN</th>
</tr>
</thead>
<tbody>
<tr>
<td>DATE/SIGN</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOCTOR SCRIPT vs. SET DOSE</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SET DOSE NO vs. MONITORED DOSE NO</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>POSITION INJECTOR MODULE</td>
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<td></td>
</tr>
<tr>
<td>Direction of arrow (down)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dry side humidifier</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inspiratory limb</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>POSITION OF SAMPLE LINE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inspiratory limb</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-15cm from pt wye</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>INOblender set up and laederal bag attached</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Check NO cylinder levels</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### APPENDIX 2: ALARMS / TROUBLESHOOTING

*Ikaria. INOmaxDSR®, Operation and maintenance manual 2013*

#### 1. High NO alarm

<table>
<thead>
<tr>
<th>Possible Cause</th>
<th>Recommended Action</th>
</tr>
</thead>
</table>
| A. Note: A newly installed NO sensor will give high readings until fully conditioned (about 5 hours) and calibrated. | a. After installation of the NO sensor perform a low and high calibration.  
b. Wait 5 hours and repeat both the low and high calibration. |
| B. The High NO alarm level may be inappropriately set. | a. Make sure the High NO alarm is set greater than the Set NO value. |
| C. The NO calibration may have drifted. | a. Perform a low and high range calibration of the NO sensor.  
b. Check calibration sample tee for leaks. |
| D. Circuit setup incorrect. | a. Check circuit setup for correct use of adapters and/or check valves. |

#### 2. Low NO alarm

<table>
<thead>
<tr>
<th>Possible Cause</th>
<th>Recommended Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. The Patient Gas Sample line may be disconnected.</td>
<td>a. Reconnect the Patient Gas Sample line.</td>
</tr>
<tr>
<td>B. The Low NO alarm setting may be inappropriately set.</td>
<td>a. Make sure the Low NO alarm is set less than the Set NO value.</td>
</tr>
<tr>
<td>C. The NO calibration may have drifted.</td>
<td>a. Perform a low and high range calibration of the NO sensor.</td>
</tr>
<tr>
<td>D. The NO sensor may not be properly seated.</td>
<td>a. Make sure the sensors are correctly seated with the O-rings and the sensor cover is fully closed.</td>
</tr>
</tbody>
</table>
| E. Loss of NO delivery. | a. If the INOblender® is available, manually ventilate the patient (see INOblender Operation Manual).  
   or  
b. Turn the backup mode ON (see page 32). |

#### 3. High NO₂ alarm

<table>
<thead>
<tr>
<th>Possible Cause</th>
<th>Recommended Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Incomplete System purge.</td>
<td>a. Perform a system purge. See Section 3/ Pre-Use Checkout.</td>
</tr>
<tr>
<td>B. Ventilator flow stopped.</td>
<td>a. Allow the ventilator gas to flush NO and NO₂ from the breathing circuit before connecting to the patient.</td>
</tr>
<tr>
<td>C. Two cylinder valves are open.</td>
<td>a. Close one of the cylinder valves.</td>
</tr>
<tr>
<td>D. The NO₂ alarm limit may be set too low.</td>
<td>a. Make sure the NO₂ alarm limit is appropriate for the Set NO level.</td>
</tr>
</tbody>
</table>
| E. The NO₂ calibration may have drifted. | a. Perform a low and high range calibration of the NO₂ sensor.  
b. Check calibration sample tee for leaks. |
| F. Out of date or the wrong calibration gas was used. | a. Verify the calibration gas expiration date.  
b. If needed replace the calibration gas and perform a low and high range calibration of the NO₂ sensor. |
| G. The patient circuit setup may be incorrect. | a. Make sure the patient circuit hoses and lengths are correct (see Section 4/ Patient Application).  
b. Verify the humidifier chamber is less than 480 mL. |
| H. Sample line occlusion. | a. Confirm whether the High NO₂ alarm occurs concurrently with a sample line block alarm.  
b. If so, this alarm will clear within 10 seconds after the sample line alarm is remedied. |
| I. The INOmax DSR® may have failed. | a. Contact Ikaria® - Technical Support.  
b. Replace the delivery system if in use.  
c. Do not use the delivery system until serviced. |
### High Priority Alarms

#### Symptom/Alarm: High O₂ alarm

<table>
<thead>
<tr>
<th>Possible Cause</th>
<th>Recommended Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. The O₂ alarm setting may be inappropriate.</td>
<td>a. Make sure the High O₂ alarm is set appropriately for the O₂ setting being used on the ventilator.</td>
</tr>
<tr>
<td>B. The O₂ calibration may have drifted.</td>
<td>a. Perform a low and high range calibration of the O₂ sensor.</td>
</tr>
<tr>
<td>C. The O₂ sensor may not be properly seated.</td>
<td>a. Make sure the sensors are correctly seated and the sensor cover is fully closed.</td>
</tr>
<tr>
<td>D. The O₂ calibration may have drifted.</td>
<td>a. Perform a low and high range calibration of the O₂ sensor.</td>
</tr>
<tr>
<td>E. The O₂ sensor may have failed.</td>
<td>a. Contact Ikaria® - Technical Support.</td>
</tr>
</tbody>
</table>

#### Symptom/Alarm: Low O₂ alarm

<table>
<thead>
<tr>
<th>Possible Cause</th>
<th>Recommended Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. The O₂ concentration setting at the ventilator was reduced.</td>
<td>a. Make sure the O₂ alarm setting is correct for the setting at the ventilator.</td>
</tr>
<tr>
<td>B. The O₂ alarm setting may be inappropriate.</td>
<td>a. The INOmax DSIR® can dilute the O₂ concentration set at the ventilator by up to 10%.</td>
</tr>
<tr>
<td>C. The O₂ sensor may not be properly seated.</td>
<td>a. Make sure the sensors are correctly seated and the sensor cover is fully closed.</td>
</tr>
<tr>
<td>D. The O₂ calibration may have drifted.</td>
<td>a. Contact Ikaria® - Technical Support.</td>
</tr>
</tbody>
</table>

#### Symptom/Alarm: Delivery Failure

<table>
<thead>
<tr>
<th>Possible Cause</th>
<th>Recommended Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Monitored NO levels ≥ 100 ppm</td>
<td>a. If the INOblender® is available, manually ventilate the patient (see INOblender Operation Manual).</td>
</tr>
<tr>
<td>B. The INOmax DSIR® has failed.</td>
<td>b. Turn the backup mode ON (see page 32).</td>
</tr>
<tr>
<td>C. INOmax DSIR® infrared cart cable is not connected or has failed.</td>
<td>c. Power the INOmax DSIR to STANDBY and then back ON to reset the delivery system. If this does not work contact Ikaria® - Technical Support.</td>
</tr>
<tr>
<td>D. INOmax DSIR® cylinder valve is closed (Delivery Stopped. The cylinder valve is closed).</td>
<td>d. Replace the delivery system if in use.</td>
</tr>
<tr>
<td>E. INOmax DSIR® cylinder not present on the INOmax DSIR® cart.</td>
<td>e. Do not use the delivery system until serviced.</td>
</tr>
</tbody>
</table>

---

Ikaria. INOmaxDSIR Operation and maintenance manual 2013
## High Priority Alarms

<table>
<thead>
<tr>
<th>Symptom/Alarm</th>
<th>Possible Cause</th>
<th>Recommended Action</th>
</tr>
</thead>
</table>
| 9. Drug Past Expiry Date Or Drug Concentration Mismatch | A. INOMAX® cylinder is expired (Delivery Stopped will occur two minutes from the point when the cylinder valve is opened). | a. Close the cylinder valve.  
b. Remove expired INOMAX cylinder from the INOMax DSIR® cart.  
c. Replace the expired INOMAX cylinder on the INOMax DSIR cart. |
|                                    | B. INOMAX cylinder is the wrong concentration (Delivery Stopped will occur two minutes from the point when the cylinder valve is opened). | a. Close the cylinder valve.  
b. Remove the INOMAX cylinder with the wrong concentration from the INOMax DSIR cart.  
c. Replace the INOMAX cylinder with the wrong concentration on the INOMax DSIR cart. |

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11 Ikaria. INOMaxDSIR, Operation and maintenance manual 2013
10. Injector Module Fail

A. The Injector Module electrical cable may be disconnected.
   - a. Reconnect the Injector Module electrical cable.
   - b. If the INOblender® is available, manually ventilate the patient (see INOblender® Operation Manual).
   - c. Turn the backup mode ON (see page 32).

B. The Injector Module may have failed.
   - a. Turn OFF the INOmax DS® set dose to silence the alarm.
   - b. If the INOblender® is available, manually ventilate the patient (see INOblender® Operation Manual).
   - c. Turn the backup mode ON (see page 32).
   - d. Replace the Injector Module.
   - e. Set the delivered dose and turn OFF the INOblender® or the backup mode.

C. The Injector Module electrical cable may have failed.
   - a. Turn OFF the INOmax DS® set dose to silence the alarm.
   - b. If the INOblender® is available, manually ventilate the patient (see INOblender® Operation Manual).
   - c. Turn the backup mode ON (see page 32).
   - d. Replace the Injector Module electrical cable.
   - e. Reset the delivered dose and turn OFF the INOblender® or the backup mode.

---

<table>
<thead>
<tr>
<th>Symptom/Alarm</th>
<th>Possible Cause</th>
<th>Recommended Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>11. Low Battery Alarm</td>
<td>A. Battery is running low (approximately 30 minutes or less until battery depletion).</td>
<td>a. Check main power indicator. b. Connect to AC main power source. c. Make sure the power cord is fully inserted into the Power Cord Inlet and that the power cord clamp is secure. d. Check and replace fuse if necessary. e. Contact Ikaria® - Technical Support.</td>
</tr>
<tr>
<td>12. Low NO/N₂ Pressure.</td>
<td>A. The NO cylinder supply may be low.</td>
<td>a. Make sure the NO cylinder is turned ON. b. If the high pressure cylinder gauge reads less than 200 psig, change the cylinder. c. If the INOblender® is available, manually ventilate the patient (see INOblender® Operation Manual).</td>
</tr>
<tr>
<td></td>
<td>B. The supply line may not be connected.</td>
<td>a. If the cylinder gauge reads greater than 200 psig: b. Verify the low pressure hoses are connected correctly to the back of the INOmax DS®. c. If the INOblender® is available, manually ventilate the patient (see INOblender® Operation Manual).</td>
</tr>
<tr>
<td></td>
<td>C. INOmax DS® has an internal leak.</td>
<td>a. Use INOblender as a stand-alone device and manually ventilate the patient (see page 105).</td>
</tr>
</tbody>
</table>

Ikaria. INOmaxDS® Operation and maintenance manual 2013
## Low Priority Alarms

<table>
<thead>
<tr>
<th>Symptom/Alarm</th>
<th>Possible Cause</th>
<th>Recommended Action</th>
</tr>
</thead>
</table>
| 15. Backup On | A. The backup mode has been turned ON and the set dose is zero. | a. Correct the reason for initiating the backup mode.  
b. Turn ON the INOmax DSIR® set dose.  
c. Turn the backup mode OFF. |
| 16. Failed NO Sensor | A. The wrong calibration gas may have been used.  
B. There is a leak around the sensors.  
C. NO sensor absent or failed. | a. Make sure the correct calibration gas is used and ensure sample tubing connections are secure and do not leak.  
b. Make sure the sensors are correctly seated with the O-rings and the sensor cover is fully closed.  
c. Replace sensor.  
b. Complete a low calibration first, and then repeat the high calibration.  
c. Replace the delivery system if in use.  
d. Contact Ikaria® - Technical Support. |
| 17. Failed NO₂ Sensor | A. The wrong calibration gas may have been used.  
B. There is a leak around the sensors.  
C. NO₂ sensor absent or failed. | a. Make sure the correct calibration gas is used and ensure sample tubing connections are secure and do not leak.  
b. Make sure the sensors are correctly seated with the O-rings and the sensor cover is fully closed.  
c. Replace sensor.  
b. Complete a low calibration first, and then repeat the high calibration.  
c. Replace the delivery system if in use.  
d. Contact Ikaria® - Technical Support. |

---

11 Ikaria. INOmaxDSIR® Operation and maintenance manual 2013
<table>
<thead>
<tr>
<th>Indicators</th>
<th>Possible Cause</th>
<th>Recommended Action</th>
</tr>
</thead>
</table>
| 23. Battery Failure | A. Communication failure with battery. | a. Connect to AC main power source.  
b. Check main power indicator.  
c. Make sure the power cord is fully inserted into the Power Cord Inlet and that the power cord clamp is secure. |
| 24. Patient Info Incomplete | A. Patient identifier has not been entered. | a. Enter patient identifier. |
| 25. Running on Battery | A. Device is operating on the battery. | a. Connect to AC main power source when available.  
b. Check main power indicator.  
c. Make sure the power cord is fully inserted into the Power Cord Inlet and that the power cord clamp is secure. |
| 26. Set Dose is Zero, Close Cylinder Valve | A. The set dose has been set to zero and the INOMAX cylinder valve is still open. | a. Close the INOMAX cylinder valve if treatment has been stopped. |

<table>
<thead>
<tr>
<th>Indicators</th>
<th>Possible Cause</th>
<th>Recommended Action</th>
</tr>
</thead>
</table>
| 18. Failed O₂ Sensor | A. The wrong calibration gas may have been used. | a. Make sure the correct calibration gas is used and ensure sample tubing connections are secure and do not leak.  
b. There is a leak around the sensors.  
c. O₂ sensor absent or failed. |
| 19. Monitoring Failure | A. Monitor is failing to communicate correctly or is reporting a fault. | a. Does not stop delivery of INOMAX® to the patient.  
b. Contact Ikaria® - Technical Support. |

<table>
<thead>
<tr>
<th>Low Priority Alarms</th>
<th>Possible Cause</th>
<th>Recommended Action</th>
</tr>
</thead>
</table>
| 20. Sample Line/Filter Block | A. The sample line may be blocked. | a. Make sure the sample inlet line and outlet ports are not obstructed.  
b. Change the sample line. |
| 21. Two Cylinders Open | A. Two cylinder valves are open. | a. Close one of the cylinder valves. |
| 22. Water Trap Bottle Full | A. The water trap bottle on the side of the INOMAX DS® is full. | a. Empty the water trap bottle.  
b. Water trap bottle is empty but the message remains in the alarm message box.  
c. The INOMAX DS® may have failed. |

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