

# Inhaled Nitric Oxide Therapy

Inhaled Nitric Oxide Therapy, or INO Therapy, was introduced in 1992 as a selective pulmonary vasodilator for term and near-term (>35 weeks) infants with hypoxemic respiratory failure (HRF). Since then, INO treatment regimens have been developed for neonates, children, and adults with Acute Respiratory Distress Syndrome (ARDS) due to pneumonia, systemic infection (sepsis), injury, inhalation of toxic substances, or aspiration of stomach contents into the lungs. INO Therapy is used to counteract HRF and ARDS by dilating the blood vessels and permitting adequate oxygenation of the blood supply.

## How Inhaled Nitric Oxide Therapy Works

Endogenous substances are used by the body to moderate blood flow through the pulmonary arteries and veins by causing these vessels to dilate (become larger). These substances stimulate the production of gaseous nitric oxide (NO) by the endothelial cells lining the lungs. Specifically, the enzyme NO synthase reacts with the amino acid L-Arginine to produce NO, which then diffuses through the pulmonary tissue into the muscle cells lining the blood vessels, where it activates another enzyme, guanylate cyclase, leading to a rise in cyclic guanosine monophosphate (cGMP) production and resulting in pulmonary vasodilation and improved ventilation/perfusion matching (V/Q). The V/Q ratio looks at the amount of air and the amount of blood reaching the alveoli, the gas-exchange structures in the lungs.

If the pulmonary vessels are constricted or obstructed, blood flow to the alveoli is reduced and the body's ability to oxygenate the blood supply becomes impaired. By supplying an inhaled source of nitric oxide, healthcare providers can use INO therapy to selectively dilate the pulmonary vessels, relieving pulmonary hypertension and improving the body's ability to absorb oxygen from inhaled air. This is significantly different to oral or IV vasodilators which will act on blood vessels throughout the body and may possibly cause a sudden and dangerous drop in blood pressure. It is the inhalation of NO, bringing it directly to the pulmonary vessels while bypassing systemic circulation, that allows it to act selectively in the pulmonary system without affecting other blood vessels in the body. Hemoglobin in the blood binds and deactivates NO, effectively blocking its effects on the rest of the body after it exits the pulmonary circulation.



## Applications for Inhaled Nitric Oxide Therapy

INO therapy can be provided to spontaneously breathing patients via a mask or nasal cannula. Neonates and patients suffering from severe ARDS are likely to be intubated and placed on a ventilator. In either case, NO from a cylinder is introduced into the gas supplied to the patient. It is generally mixed with room air, and often with additional oxygen to help relieve hypoxia until the nitric oxide has had the desired vasodilatory effect.

The FDA considers nitric oxide to be a drug, and regulates its use accordingly. Safety and toxicity concerns necessitate continuous and careful monitoring of the dosage being supplied to the patient. High levels (>5,000 ppm) can be lethal, but those in the normal therapeutic range (1-80 ppm) appear to be safe for even long term exposure. Additionally, NO can react with O<sub>2</sub> to produce the toxic chemical NO<sub>2</sub> (nitrogen dioxide), so the precise delivery of the lowest effective levels of NO is key, especially in situations dictating high levels of oxygen. A sensitive, accurate, and reliable monitoring system that can measure single ppm levels of NO, NO<sub>2</sub>, and O<sub>2</sub> is a critical component of any INO system.

## Challenges Associated with Inhaled Nitric Oxide Therapy

The nitric oxide gas in the cylinder is extremely dry, which can strip moisture from the mucous membranes lining the breathing passages and lungs, leading to patient discomfort and increasing the risk of infection. A bubbler-type humidifier is thus included in the breathing circuit to add moisture to the gas mixture supplied to the patient. In such systems, the breathing mixture flows across or bubbles through a heated water bath maintained at 37°C.

This method greatly increases patient comfort, but also complicates accurate measurement of the therapeutic gases. The portion of the gas mixture that flows to the monitoring system must have the humidity reduced to room air levels in order to prevent condensation. If condensation reaches the analyzer, it will cause irreparable harm to the sensor and render the equipment unusable.

## The Perma Pure Solution: ME Series Highly – Selective Permeation Tubing

When Perma Pure's ME Series moisture exchangers are included in the sample line, excess moisture is removed while preserving the sample integrity. The ME Series utilizes Nafion® technology to remove only water vapor without changing the levels or concentrations of NO, NO<sub>2</sub>, or O<sub>2</sub>. Some systems also include a water trap immediately prior to the entry point into the sensor enclosure. Using an ME Series moisture exchanger in the sample line will greatly reduce the amount of residual moisture, extending the time between drainings/cleanings of the water trap. Additionally, warm, moist air provides an ideal environment for the growth of microorganisms such as bacteria and viruses which can collect and grow in the trap over time, increasing the risk of ventilator acquired pneumonia and other nosocomial infections. Some customers have even eliminated the water trap in their systems, relying on ME Series products to remove enough moisture to protect the sensor.

## Delivering the Perma Pure Medical Advantage for Breath Drying

- Fast response time – instantaneous and continuous moisture transfer
- Fully bio-compatible for surface contact with patient skin
- Utilizes Nafion® membrane tubing technology
- Removes up to 90% of moisture
- Improves accuracy of IR-based EtCO<sub>2</sub> measurements by eliminating moisture interference
- Highly selective – removes water vapor while retaining sample analytes
- Prevents condensation to protect medical monitoring equipment
- Reduces dead volume in sample circuit when compared with a water traps

For more than forty years, Perma Pure has provided solutions for managing moisture in critical applications related to health and environmental safety. Our medical solutions include highly-selective permeation tubing products which are used by industry leading OEMs of medical diagnostic equipment and patient consumable products. We are proud to partner with our broad and diverse customer base to make the world healthier and cleaner. Our commitment to protect life starts with a focus on quality and partnership with our customers to meet the challenges of a dynamic global marketplace while making the world safer and healthier.

Perma Pure is the exclusive manufacturer of Nafion® tubing, a highly-selective permeation membrane that is uniquely suited for medical moisture management. It can be used to remove moisture from breath samples prior to analysis. Our Nafion®-based solutions take advantage of the material's unique properties that allow the removal of water vapor without the loss of any other compounds, such as CO<sub>2</sub> or anesthetic agents. Removal of moisture improves accuracy of IR-based CO<sub>2</sub> measurements by eliminating interference.

## Providing the Highest Quality and Reliability

We are a proven supplier to industry-leading medical device OEMs. Our manufacturing process and quality meet the high standards required for medical applications.

- 100% leak and flow testing of dryers and sample lines
- ISO9001 and ISO13485 certified
- FDA registered
- ISO14644 Class 8 cleanroom manufacturing
- Braided polypropylene monofilament protects Nafion® tubing
- Flexible for easier integration into the module
- Kink-resistant for bending and coiling

## Offering Advanced Assembly Services

More than just tubing – we offer a full array of assembly capabilities to meet your specifications.

- Sample lines with or without dryers
- Custom labeling and packaging
- Design optimization for better flow and moisture exchange
- Standard or custom connectors
- Test capabilities
- Overmolding and solvent bonding of connectors

## A Quality-Driven, Innovative Partner

Perma Pure is a trusted supplier to thousands of customers. Our Nafion®-based solutions have enabled our customers to reduce cost, improve reliability, increase accuracy, and bring new and innovative medical products to market. You can turn to Perma Pure with confidence for proven moisture management solutions, backed by decades of experience, to enable your next breakthrough.

# Serving a Wide Range of Applications

Perma Pure ME Series products are an enabling technology for:

CAPNOGRAPHY • ANESTHESIA MONITORING • PULMONARY FUNCTION TESTING • INHALED GAS THERAPY

Part #	
<b>ME Moisture Exchanger Series</b>	<b>ME</b>
<b>Nafion® Tubing Size and Typical Sample Flow Rates</b>	
1.07mm ID x 1.35mm OD – samples up to 200cc/min	50
1.32 ID x 1.60mm OD – samples up to 400cc/min	60
1.52mm ID x 1.83mm OD – samples up to 600cc/min	70
2.18mm ID x 2.74mm OD – samples up to 1L/min	110
<b>Standard Dryer Lengths</b>	
6" (15 cm)	6
12" (30 cm)	12
18" (45cm)	18
24" (60 cm)	24
48" (120 cm)	48
<b>End Fittings</b>	
DEHP-free medical tubing attached to each end of ME Series	TT
Thermoplastic tube with nylon barb coupling	BT
Nylon barbed fitting (ME-070 and ME-110 only)	BB
1/16" molded polypropylene barb fitting (ME-050, ME-060 only)	MB
Stainless steel tube in molded polypropylene header	ST
Molded male locking luer fitting (not available on ME-110)	ML
Male locking luer with push-in barb attached with heat shrink	BML
Molded female luer fitting (not available on ME-110)	FL
Female locking luer with push-in barb attached with heat shrink	BFL
Molded male slip luer fitting (not available on ME-110)	MS
With 1/8" stainless steel compression fittings (ME-060 only)	COMP2
Molded headers for 1/4" compression fittings (ME-110 only)	COMP4



ME	050	12	BB
Series	Tubing	Length	Fittings