GENOSYL- nitric oxide gas
VERO BIOTECH, INC.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use GENOSYL ®safely and effectively. See full prescribing information for GENOSYL. GENOSYL (nitric oxide), for inhalation use
Initial U.S. Approval: 1999

INDICATIONS AND USAGE

GENOSYL is a vasodilator indicated to improve oxygenation and reduce the need for extracorporeal membrane oxygenation in term and near-term (>34 weeks gestation) neonates with hypoxic respiratory failure associated with clinical or echocardiographic evidence of pulmonary hypertension in conjunction with ventilatory support and other appropriate agents (1).

DOSAGE AND ADMINISTRATION

The recommended dose is 20 ppm, maintained for up to 14 days or until the underlying oxygen desaturation has resolved (2.1).
Doses greater than 20 ppm are not recommended (2.1, 5.2).
Administration: Avoid abrupt discontinuation (2.2, 5.1).

DOSAGE FORMS AND STRENGTHS

GENOSYL (nitric oxide) is a gas, available at concentrations up to 800 ppm. (3)

CONTRAINDICATIONS

Neonates dependent on right-to-left shunting of blood (4).

WARNINGS AND PRECAUTIONS

Rebound Pulmonary Hypertension: Abrupt discontinuation of GENOSYL may lead to worsening oxygenation and increasing pulmonary artery pressure (5.1).
Methemoglobinemia: Methemoglobin increases with the dose of nitric oxide; following discontinuation or reduction of nitric oxide, methemoglobin levels return to baseline over a period of hours (5.2).
Elevated NO_2Levels: Monitor NO_2levels (5.3).
Heart Failure: In patients with pre-existing left ventricular dysfunction, GENOSYL may increase pulmonary capillary wedge pressure leading to pulmonary edema (5.4).

ADVERSE REACTIONS

The most common adverse reaction is hypotension (6).
To report SUSPECTED ADVERSE REACTIONS, contact Vero Biotech at 1-877-337-4118 and http://www.vero-biotech.com/ or FDA at 1-800-FDA-1088 orwww.fda.gov/medwatch.

DRUG INTERACTIONS

Nitric oxide donor compounds may increase the risk of developing methemoglobinemia (7).

Revised: 12/2022

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

GENOSYL ®is indicated to improve oxygenation and reduce the need for extracorporeal membrane oxygenation in term and near-term (>34 weeks gestation) neonates with hypoxic respiratory failure associated with clinical or echocardiographic evidence of pulmonary hypertension in conjunction with ventilatory support and other appropriate agents.

2 DOSAGE AND ADMINISTRATION

2.1 Dosage

Term and near-term neonates withhypoxic respiratory failure

The recommended dose of GENOSYL is 20 ppm. Maintain treatment up to 14 days or until the underlying oxygen desaturation has resolved and the neonate is ready to be weaned from GENOSYL therapy.

Doses greater than 20 ppm are not recommended *[see Warnings and Precautions (5.2)].*

2.2 Administration

Nitric OxideDelivery System

GENOSYL must be administered using a calibrated GENOSYL Delivery System. Only validated ventilator systems should be used in conjunction with GENOSYL *[see Description (11)].*

Consult the GENOSYL Delivery System Operator's Manual or call 1-877-337-4118 or visit www.vero-biotech.comfor needed information on training and technical support for users of GENOSYL with the GENOSYL Delivery System .

Keep available a backup power supply to address power failures. The GENOSYL Delivery System consists of a primary system and a fully functional second system that can be used as backup in the event of primary system failure.

Monitoring

Measure methemoglobin within 4-8 hours after initiation of treatment with GENOSYL and periodically throughout treatment *[see Warnings and Precautions (5.2)].*

Monitor for PaO_2 and inspired NO_2 during GENOSYL administration *[see Warnings and Precautions (5.3)].*

Weaning and Discontinuation

Avoid abrupt discontinuation of GENOSYL *[see Warnings and Precautions (5.1)].* To wean GENOSYL, down titrate in several steps, pausing several hours at each step to monitor for hypoxemia.

3 DOSAGE FORMS AND STRENGTHS

GENOSYL (nitric oxide) is a gas available at concentrations up to 800 ppm *[see Description (11)]* .

4 CONTRAINDICATIONS

GENOSYL is contraindicated in neonates dependent on right-to-left shunting of blood.

5 WARNINGS AND PRECAUTIONS

5.1 Rebound Pulmonary Hypertension Syndrome following Abrupt Discontinuation

Wean from GENOSYL *[see Dosage and Administration (2.2)].* Abrupt discontinuation of GENOSYL may lead to worsening oxygenation and increasing pulmonary artery pressure, i.e., Rebound Pulmonary Hypertension Syndrome. Signs and symptoms of Rebound Pulmonary Hypertension Syndrome include hypoxemia, systemic hypotension, bradycardia, and decreased cardiac output. If Rebound Pulmonary Hypertension occurs, reinstate GENOSYL therapy immediately.

5.2 Hypoxemia from Methemoglobinemia

Nitric oxide combines with hemoglobin to form methemoglobin, which does not

transport oxygen. Methemoglobin levels increase with the dose of GENOSYL; it can take 8 hours or more before steady-state methemoglobin levels are attained. Monitor methemoglobin and adjust the dose of GENOSYL to optimize oxygenation.

If methemoglobin levels do not resolve with decrease in dose or discontinuation of GENOSYL, additional therapy may be warranted to treat methemoglobinemia *[see Overdosage (10)]* .

5.3 Airway Injury from Nitrogen Dioxide

Nitrogen dioxide (NO_2) forms in gas mixtures containing NO and O_2. Nitrogen dioxide may cause airway inflammation and damage to lung tissues.

If there is an unexpected change in NO_2concentration, or if the NO_2concentration reaches 0.5 ppm when measured in the breathing circuit, then the delivery system should be assessed in accordance with the GENOSYL Delivery System Operator's Manual troubleshooting section, and the NO_2analyzer should be recalibrated. The dose of GENOSYL and/or FiO_2should be adjusted as appropriate.

5.4 Worsening Heart Failure

Patients with left ventricular dysfunction treated with GENOSYL may experience pulmonary edema, increased pulmonary capillary wedge pressure, worsening of left ventricular dysfunction, systemic hypotension, bradycardia and cardiac arrest. Discontinue GENOSYL while providing symptomatic care.

6 ADVERSE REACTIONS

The following adverse reactions are discussed elsewhere in the label;

Hypoxemia *[see Warnings and Precautions (5.2)]*

Worsening Heart Failure *[see Warnings and Precautions (5.4)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. The adverse reaction information from the clinical studies does, however, provide a basis for identifying the adverse events that appear to be related to drug use and for approximating rates.

Controlled studies have included 325 patients on nitric oxide doses of 5 to 80 ppm and 251 patients on placebo. Total mortality in the pooled trials was 11% on placebo and 9% on nitric oxide gas for inhalation, a result adequate to exclude nitric oxide mortality being more than 40% worse than placebo.

In both the NINOS and CINRGI studies, the duration of hospitalization was similar in nitric oxide gas for inhalation and placebo-treated groups.

From all controlled studies, at least 6 months of follow-up is available for 278 patients who received nitric oxide gas and 212 patients who received placebo. Among these patients, there was no evidence of an adverse effect of treatment on the need for re-

hospitalization, special medical services, pulmonary disease, and neurological sequelae.

In the NINOS study, treatment groups were similar with respect to the incidence and severity of intracranial hemorrhage, Grade IV hemorrhage, periventricular leukomalacia, cerebral infarction, seizures requiring anticonvulsant therapy, pulmonary hemorrhage, or gastrointestinal hemorrhage.

In CINRGI, the only adverse reaction (>2% higher incidence on nitric oxide gas for inhalation than on placebo) was hypotension (14% vs. 11%).

6.2 Post-Marketing Experience

Post marketing reports of accidental exposure to nitric oxide for inhalation in hospital staff have been associated with chest discomfort, dizziness, dry throat, dyspnea, and headache.

7 DRUG INTERACTIONS

7.1 Nitric Oxide Donor Agents

Nitric oxide donor agents such as prilocaine, sodium nitroprusside and nitroglycerine may increase the risk of developing methemoglobinemia.

8 USE IN SPECIFIC POPULATIONS

8.4 Pediatric Use

The safety and efficacy of nitric oxide for inhalation has been demonstrated in term and near-term neonates with hypoxic respiratory failure associated with evidence of pulmonary hypertension *[see Clinical Studies (14.1)]* . Additional studies conducted in premature neonates for the prevention of bronchopulmonary dysplasia have not demonstrated substantial evidence of efficacy *[see Clinical Studies (14.3)]* . No information about its effectiveness in other age populations is available.

8.5 Geriatric Use

Nitric oxide is not indicated for use in the adult population.

10 OVERDOSAGE

Overdosage with nitric oxide gas is manifest by elevations in methemoglobin and pulmonary toxicities associated with inspired NO_2. Elevated NO_2 may cause acute lung injury. Elevations in methemoglobin reduce the oxygen delivery capacity of the circulation. In clinical studies, NO_2 levels >3 ppm or methemoglobin levels >7% were treated by reducing the dose of, or discontinuing, nitric oxide gas.

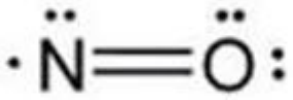
Methemoglobinemia that does not resolve after reduction or discontinuation of therapy can be treated with intravenous vitamin C, intravenous methylene blue, or blood transfusion, based upon the clinical situation.

11 DESCRIPTION

GENOSYL (nitric oxide) is administered by inhalation. Nitric oxide is a pulmonary vasodilator. Nitric oxide is generated from liquid dinitrogen tetroxide (N_2O_4) by the cassette in the GENOSYL Delivery System. Upon initiation of GENOSYL Delivery System, the liquid N_2O_4 is heated and the equilibrium shifts to nitrogen dioxide (NO_2) gas. The NO_2 is then converted into nitric oxide (NO) using the antioxidant cartridges, and nitric oxide is delivered to the patient by means of a ventilator or a nasal cannula. The amount of nitric oxide administered to the patient is set by controlling the temperature of the N_2O_4 liquid module, which controls the pressure inside the liquid module, which in turn controls the mass of NO_2 that is sent to the primary cartridges, and hence the mass of nitric oxide. The mass flow of nitric oxide, together with the air from the pump, control the nitric oxide concentration. A nitric oxide sensor monitors the nitric oxide in the patient line. GENOSYL Delivery System is designed to deliver a controlled level of nitric oxide blended with breathing air or oxygen-enriched breathing air.

The GENOSYL Delivery System controls the flow of nitric oxide mixed with air delivered to the patient.

The structural formula of nitric oxide (NO) is shown below:



12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Nitric oxide relaxes vascular smooth muscle by binding to the heme moiety of cytosolic guanylate cyclase, activating guanylate cyclase and increasing intracellular levels of cyclic guanosine 3',5'-monophosphate, which then leads to vasodilation. When inhaled, nitric oxide selectively dilates the pulmonary vasculature, and because of efficient scavenging by hemoglobin, has minimal effect on the systemic vasculature.

GENOSYL appears to increase the partial pressure of arterial oxygen (PaO_2) 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.

12.2 Pharmacodynamics

Effects on Pulmonary Vascular Tone in PPHN

Persistent pulmonary hypertension of the newborn (PPHN) occurs as a primary developmental defect or as a condition secondary to other diseases such as meconium aspiration syndrome (MAS), pneumonia, sepsis, hyaline membrane disease, congenital diaphragmatic hernia (CDH), and pulmonary hypoplasia. In these states, pulmonary vascular resistance (PVR) is high, which results in hypoxemia secondary to right-to-left shunting of blood through the patent ductus arteriosus and foramen ovale. In neonates with PPHN, nitric oxide gas for inhalation improves oxygenation (as indicated by significant increases in PaO_2).

12.3 Pharmacokinetics

The pharmacokinetics of nitric oxide has been studied in adults.

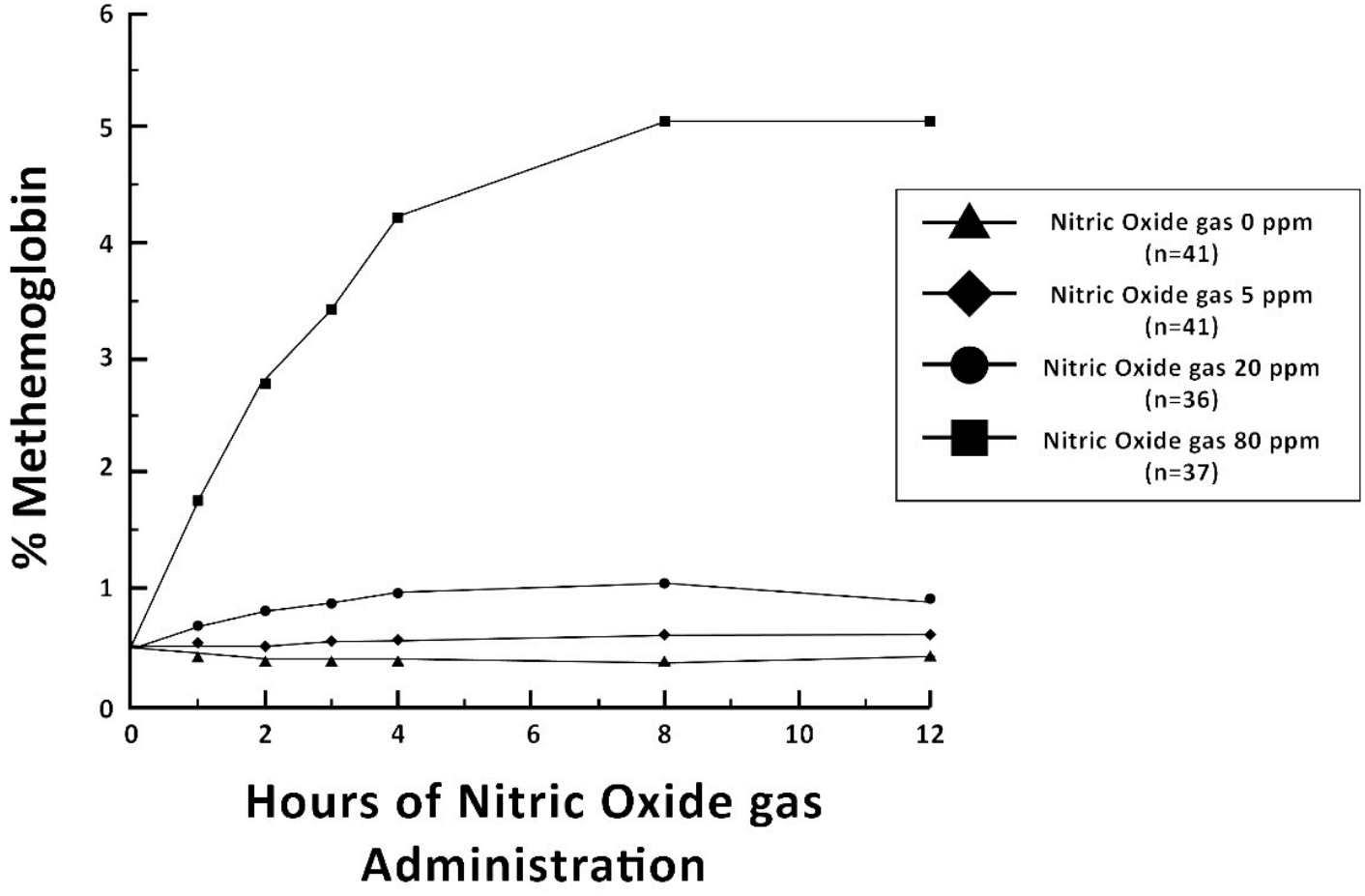
Absorption and Distribution

Nitric oxide is absorbed systemically after inhalation. Most of it traverses the pulmonary capillary bed where it combines with hemoglobin that is 60% to 100% oxygen-saturated. At this level of oxygen saturation, nitric oxide combines predominantly with oxyhemoglobin to produce methemoglobin and nitrate. At low oxygen saturation, nitric oxide can combine with deoxyhemoglobin to transiently form nitrosylhemoglobin, which is converted to nitrogen oxides and methemoglobin upon exposure to oxygen. Within the pulmonary system, nitric oxide can combine with oxygen and water to produce nitrogen dioxide and nitrite, respectively, which interact with oxyhemoglobin to produce methemoglobin and nitrate. Thus, the end products of nitric oxide that enter the systemic circulation are predominantly methemoglobin and nitrate.

Metabolism

Methemoglobin disposition has been investigated as a function of time and nitric oxide exposure concentration in neonates with respiratory failure. The methemoglobin (MetHb) concentration-time profiles during the first 12 hours of exposure to 0, 5, 20, and 80 ppm nitric oxide are shown in Figure 1.

Figure 1 : Methemoglobin Concentration - Time Profiles Neonates Inhaling 0, 5, 20 or 80 ppm Nitric Oxide gas



Methemoglobin concentrations increased during the first 8 hours of nitric oxide exposure. The mean methemoglobin level remained below 1% in the placebo group and in the 5 ppm and 20 ppm nitric oxide gas groups, but reached approximately 5% in the 80 ppm nitric oxide gas group. Methemoglobin levels >7% were attained only in patients receiving 80 ppm, where they comprised 35% of the group. The average time to reach peak methemoglobin was 10 ± 9 (SD) hours (median, 8 hours) in these 13 patients, but one patient did not exceed 7% until 40 hours.

Elimination

Nitrate has been identified as the predominant nitric oxide metabolite excreted in the urine, accounting for >70% of the nitric oxide dose inhaled. Nitrate is cleared from the plasma by the kidney at rates approaching the rate of glomerular filtration.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No evidence of a carcinogenic effect was apparent, at inhalation exposures up to the recommended dose (20 ppm), in rats for 20 hr/day for up to two years. Higher exposures have not been investigated.

Nitric oxide gas has demonstrated genotoxicity in Salmonella (Ames Test), human lymphocytes, and after in vivo exposure in rats. There are no animal or human studies to evaluate nitric oxide for effects on fertility.

14 CLINICAL STUDIES

14.1 Treatment of Hypoxic Respiratory Failure (HRF)

The efficacy of nitric oxide gas was investigated in term and near-term newborns with hypoxic respiratory failure (HRF) resulting from a variety of etiologies. Inhalation of nitric oxide gas reduces the oxygenation index (OI= mean airway pressure in cm H_2O × fraction of inspired oxygen concentration [FiO_2]× 100 divided by systemic arterial concentration in mm Hg [PaO_2]) and increases PaO_2 *[see Clinical Pharmacology (12.1)]* .

NINOS Study

The Neonatal Inhaled Nitric Oxide Study (NINOS) was a double-blind, randomized, placebo-controlled, multicenter trial in 235 neonates with hypoxic respiratory failure. The objective of the study was to determine whether inhaled nitric oxide would reduce the occurrence of death and/or initiation of extracorporeal membrane oxygenation (ECMO) in a prospectively defined cohort of term or near-term neonates with hypoxic respiratory failure unresponsive to conventional therapy. Hypoxic respiratory failure was caused by meconium aspiration syndrome (MAS; 49%), pneumonia/sepsis (21%), idiopathic primary pulmonary hypertension of the newborn (PPHN; 17%), or respiratory distress syndrome (RDS; 11%). Infants ≤14 days of age (mean, 1.7 days) with a mean $PaO_2$of 46 mmHg and a mean oxygenation index (OI) of 43 cm H_2O / mmHg were initially randomized to receive 100% $O_2$with (n=114) or without (n=121) 20 ppm nitric oxide for up to 14 days. Response to study drug was defined as a change from baseline

in PaO_2 30 minutes after starting treatment (full response = >20 mmHg, partial = 10-20 mmHg, no response = <10 mmHg). Neonates with a less than full response were evaluated for a response to 80 ppm nitric oxide or control gas. The primary results of this study are presented in Table 1.

Table 1: Summary of Clinical Results from Hypoxic Respiratory Failure Study

	Control (n=121)	Nitric Oxide gas (n=114)	P value
Death or ECMO *†	77 (64%)	52 (46%)	0.006
Death	20 (17%)	16 (14%)	0.60
ECMO	66 (55%)	44 (39%)	0.014

* Extracorporeal membrane oxygenation
† Death or need for ECMO was the parimary end point of this study

Although the incidence of death by 120 days of age was similar in both groups (NO, 14%; control 17%), significantly fewer infants in the nitric oxide group required ECMO compared with controls (39% vs. 55%, p = 0.014). The combined incidence of death and/or initiation of ECMO showed a significant advantage for the nitric oxide treated group (46% vs. 64%, p = 0.006). The nitric oxide group also had significantly greater increases in PaO_2 and greater decreases in the OI and the alveolar-arterial oxygen gradient than the control group (p<0.001 for all parameters). Significantly more patients had at least a partial response to the initial administration of study drug in the nitric oxide group (66%) than the control group (26%, p<0.001). Of the 125 infants who did not respond to 20 ppm nitric oxide control, similar percentages of NO-treated (18%) and control (20%) patients had at least a partial response to 80 ppm nitric oxide gas for inhalation or control drug, suggesting a lack of additional benefit for the higher dose of nitric oxide. No infant had study drug discontinued for toxicity. Inhaled nitric oxide gas had no detectable effect on mortality. The adverse events collected in the NINOS trial occurred at similar incidence rates in both treatment groups *[see Adverse Reactions (6.1)]* . Follow-up exams were performed at 18-24 months for the infants enrolled in this trial. In the infants with available follow-up, the two treatment groups were similar with respect to their mental, motor, audiologic, or neurologic evaluations.

CINRGI Study

This study was a double-blind, randomized, placebo-controlled, multi-center trial of 186 term and near-term neonates with pulmonary hypertension and hypoxic respiratory failure. The primary objective of the study was to determine whether nitric oxide gas would reduce the receipt of ECMO in these patients. Hypoxic respiratory failure was caused by MAS (35%), idiopathic PPHN (30%), pneumonia/sepsis (24%), or RDS (8%). Patients with a mean PaO_2 of 54 mmHg and a mean OI of 44 cm H_2O / mmHg were randomly assigned to receive either 20 ppm nitric oxide gas (n=97) or nitrogen gas (placebo; n=89) in addition to their ventilatory support. Patients who exhibited a PaO_2 >60 mmHg and a pH < 7.55 were weaned to 5 ppm nitric oxide gas or placebo. The primary results from the CINRGI study are presented in Table 2.

Table 2: Summary of Clinical Results from Persistent Pulmonary Hypertension of the Newborn Study

	Placebo	Nitric oxide gas	P value
ECMO *†	51/89 (57%)	30/97 (31%)	<0.001
Death	5/89 (6%)	3/97 (3%)	0.48

* Extracorporeal membrane oxygenation
† ECMO was the primary end point of this study

Significantly fewer neonates in the nitric oxide gas group required ECMO compared to the control group (31% vs. 57%, p<0.001). While the number of deaths were similar in both groups (Nitric oxide gas, 3%; placebo, 6%), the combined incidence of death and/or receipt of ECMO was decreased in the nitric oxide gas group (33% vs. 58%, p<0.001).

In addition, the nitric oxide gas group had significantly improved oxygenation as measured by PaO_2, OI, and alveolar-arterial gradient (p<0.001 for all parameters). Of the 97 patients treated with nitric oxide gas, 2 (2%) were withdrawn from study drug due to methemoglobin levels >4%. The frequency and number of adverse events reported were similar in the two study groups *[see Adverse Reactions (6.1)]* .

In clinical trials, reduction in the need for ECMO has not been demonstrated with the use of inhaled nitric oxide in neonates with congenital diaphragmatic hernia (CDH).

14.2 Ineffective in Adult Respiratory Distress Syndrome (ARDS)

In a randomized, double-blind, parallel, multicenter study, 385 patients with adult respiratory distress syndrome (ARDS) associated with pneumonia (46%), surgery (33%), multiple trauma (26%), aspiration (23%), pulmonary contusion (18%), and other causes, with PaO_2/FiO_2<250 mmHg despite optimal oxygenation and ventilation, received placebo (n=193) or nitric oxide gas (n=192), 5 ppm, for 4 hours to 28 days or until weaned because of improvements in oxygenation. Despite acute improvements in oxygenation, there was no effect of nitric oxide gas on the primary endpoint of days alive and off ventilator support. These results were consistent with outcome data from a smaller dose ranging study of nitric oxide (1.25 to 80 ppm). GENOSYL (nitric oxide) for inhalation is not indicated for use in ARDS.

14.3 Ineffective in Prevention of Bronchopulmonary Dysplasia (BPD)

The safety and efficacy of nitric oxide gas for the prevention of chronic lung disease [bronchopulmonary dysplasia (BPD)] in neonates ≤ 34 weeks gestational age requiring respiratory support has been studied in four large previously conducted multicenter, double-blind, placebo-controlled clinical trials in a total of 2,600 preterm infants. Of these, 1,290 received placebo, and 1,310 received inhaled nitric oxide at doses ranging from 5-20 ppm, for treatment periods of 7-24 days duration. The primary endpoint for these studies was alive and without BPD at 36 weeks postmenstrual age (PMA). The need for supplemental oxygen at 36 weeks PMA served as a surrogate endpoint for the presence of BPD. Overall, efficacy for the prevention of bronchopulmonary dysplasia in preterm infants was not established. There were no meaningful differences between treatment groups with regard to overall deaths, methemoglobin levels, or adverse

events commonly observed in premature infants, including intraventricular hemorrhage, patent ductus arteriosus, pulmonary hemorrhage, and retinopathy of prematurity.

The use of GENOSYL (nitric oxide) for prevention of BPD in preterm neonates ≤34 weeks gestational age is not recommended.

16 HOW SUPPLIED/STORAGE AND HANDLING

GENOSYL Delivery System cassettes produce at least 216 liters of 800 ppm nitric oxide gas (at standard temperature and pressure, STP) (NDC 72385-002-01).

Store at 20°C to 25°C (68°F to 77°F) with excursions permitted between 15°C and 30°C (59°F and 86°F) [see USP Controlled Room Temperature].

The GENOSYL Delivery System must be used with antioxidant cartridges not older than 12 months from the manufacturing date.

Occupational Exposure

The exposure limit set by the Occupational Safety and Health Administration (OSHA) for nitric oxide is 25 ppm, and for NO_2 the limit is 5ppm.

Rx Only

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VĒRO
BIOTECH

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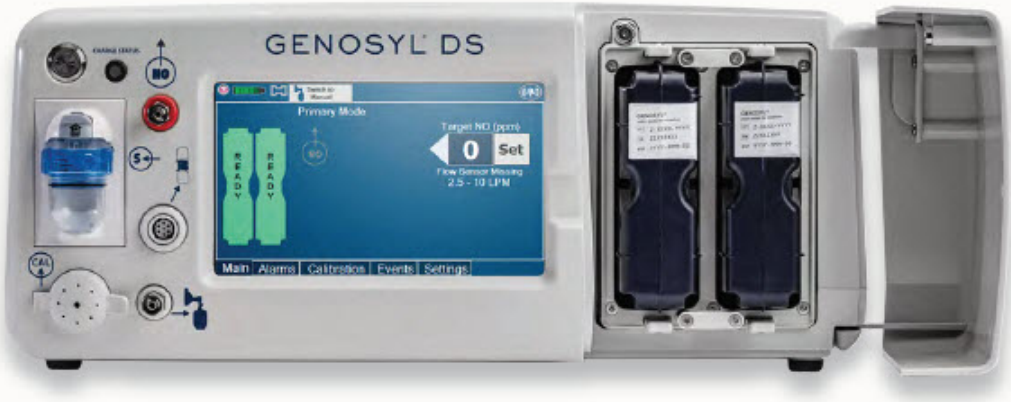
GENOSYL®

DELIVERY SYSTEM



FOR DELIVERY OF

GENOSYL®

(NITRIC OXIDE)
GAS FOR INHALATION

OPERATOR'S MANUAL

Technical Support: 877.337.4118

Company Confidential
Part No. 602502 Rev. D

DO NOT COPY

Vero Biotech Inc.

387 Technology Circle NW, Suite 125
Atlanta, GA 30313 USA

WARNINGS, CAUTIONS, AND NOTES

Please read all warnings and cautions in this Operator's Manual prior to using the GENOSYL DS.

MR Conditional Safety Information

The GENOSYL DS may be safely used in the MR environment under the following conditions. Failure to follow these conditions may result in injury.

- Maximum static magnetic field of 100 Gauss (0.01mT)
- Device remains outside the scanner bore
- Preparation protocols described in the Warnings section titled "Use in the MR Environment" must be followed before MR procedure

Image Artifacts:

When the GENOSYL DS is battery powered, no image artifacts are expected. When powered using a wall outlet, minor noise is expected.

Throughout this Operator's Manual, warning, cautions, and notes will be displayed in the following manner.

WARNING
The warning box will alert the user to possible injury, death, or serious adverse reactions associated with the use or misuse of the device.

CAUTION
The caution box will alert the user about proper use of the equipment and any conditions that could result in equipment damage or failure. The user should read and adhere to all warnings and cautions.

NOTE
The note box provides information, clarification, or supplemental information to assist and educate the user on the use of the equipment.

A complete list of Warnings and Cautions for the GENOSYL DS are shown below. Where appropriate, some of these will also be shown throughout this manual.

WARNINGS

Please consult the package insert for a complete list of contraindications.

Alarms

- ALWAYS acknowledge and follow information provided from alarms. An alarm indicates an abnormal condition, and ignoring alarms can result in possible injury, death, or serious adverse reactions.
- ALWAYS use clinical judgement when setting upper or lower alarm limits. Failure to do so could result in possible injury or death.

Consoles

- ALWAYS have a second Console present and properly connected when a Dosing Console is connected to the patient. If the Dosing Console malfunctions, switch to the Back-up Console. If the Back-up Console is not available or properly connected, this may result in patient injury or death.
- DO NOT clean the GENOSYL DS with the power connected and the System turned ON, as this may lead to injury (e.g., shock). Unplug AC/DC power supply external to the System prior to cleaning.
- NEVER modify the equipment. Modifications of the equipment may result in malfunction, which may result in a fire, shock, injury, or death.
- NEVER turn the rear power switch OFF until the System has gone through a controlled shutdown or instructed by VERO Technical Support. Turning the rear power switch OFF prematurely (e.g., while it is still in use) will immediately shut down the device. This may result in interruption in NO delivery to the patient, which may cause injury or death.

Cassette

- DO NOT use the Cassette if the Cassette State Window is not blue. A Cassette State Window that is any color other than blue may affect the Cassette's ability to provide the correct NO dosage to the patient, which may cause injury or death.
- DO NOT use a Cassette that is beyond its expiration date. Using an expired Cassette may affect the Cassette's ability to provide the correct NO dosage to the patient, which may cause injury or death.
- MAKE SURE the System stabilizes to the prescribed concentration (ppm) of NO prior to leaving the Console unattended. Failure to do so could result in under delivery of the target NO, leading to injury or harm.
- ALWAYS replace a Cassette once depleted. A depleted Cassette will interrupt patient dosing and can lead to under dosing and/or injury to the patient.
- ALWAYS follow Cassette inspection instructions prior to Cassette insertion. Not inspecting the Cassette prior to insertion may lead to using a faulty Cassette, resulting in injury.

Use in the MR Environment

- The GENOSYL DS is classified as MR Conditional with MR scanners of 1.5 or 3.0 Tesla strength ONLY in areas where the field strength is less than 100 gauss.
- ALWAYS operate at a fringe field of less than 100 gauss. This device contains ferromagnetic components and may experience strong attraction close to the magnet.
- DO NOT exceed 100 gauss; System operation may be impacted. Confirm Cart caster lock function. Optionally connect tether.
- NEVER use the GENOSYL DS in the MR scanner room without gauss alarms installed.

- ALWAYS verify at least one gauss alarm is functioning properly prior to use in the MR environment.
- DO NOT use the GENOSYL DS in the MR environment if neither gauss alarm is functional.
- ALWAYS move System away from the MR scanner if the gauss alarm sounds. The gauss alarm will sound if the System is too close to the MR scanner. Move System away from the MR scanner until the gauss alarm stops sounding.
- ALWAYS verify that the GENOSYL DS Cart casters are locked after positioning the System in the MR scanner room.
- ALWAYS verify that the GENOSYL DS is securely attached to the Cart.
- ALWAYS arrange power cord, MR patient gas sample line, and NO delivery line to avoid entanglement, strangulation and/or a trip hazard.
- DO NOT use the GENOSYL DS in the MR environment if the Cart moves when the brake caster locks are engaged.
- NEVER perform NO or NO_2 calibration within the MR scanner room. Calibration equipment is a potential projectile hazard.

Connections
- ALWAYS follow pre-use setup instructions for the routing and connections of tubing to avoid patient strangulation.
- MAKE SURE the System has all tubing connected as described in the instructions. Not connecting all tubing may result in inaccurate dosage and harm the patient.
- NEVER touch the electrical connectors of the System or its accessories, and the patient simultaneously. If the user touches another device with a ground-fault failure and simultaneously touches the GENOSYL DS, this can result in injury (e.g., shock) should a grounding failure be present.

Battery
- ONLY properly trained personnel should replace the battery. Incorrectly replacing the battery may result in a hazard such as excessive temperatures, fire, or explosion.
- MAKE SURE the GENOSYL DS is connected to AC wall power to charge the battery a minimum of once every 3 months to maintain a minimum battery charge. Failure to recharge the Console battery for extended timeframes may result in full discharge of the battery. If a Battery Error message occurs during startup of the System, contact Technical Support at 877-337-4118 for assistance.

User
- ONLY intended users who are experienced in the use of this System should use this device. US federal law restricts device use to licensed medical professionals. If device is used by unintended users, device can be misused and lead to injury or death.

Alternative Means of Ventilation
- ALWAYS ensure that the manual flow displayed on the Console matches the flow set into the resuscitation bag. Incorrect flow settings may result in an incorrect estimation of NO delivery. If the flow into the manual equipment is too low, there is risk of overdosing the patient with NO.
- ALWAYS squeeze the bag several times, after starting fresh gas flow, to empty residual gas in the bag prior to using the System to ventilate a patient. Failure to do so could result in higher NO_2 levels being delivered to the patient.

- ALWAYS use the smallest bag adequate to deliver the desired tidal volume. Failure to do so could result in higher NO_2 levels being delivered to the patient.

Patient Monitoring

- ALWAYS constantly monitor the patient. System malfunctions can occur if device and patient are not monitored and can result in injury or death. Careful monitoring is required by care personnel whenever the System is used on a patient. The use of an alarm and a monitoring system does not give an absolute assurance of warning for every malfunction that may occur. Certain alarms may require immediate response.

Use with Breathing Devices

- DO NOT use the GENOSYL DS with circle anesthesia ventilator systems. The GENOSYL DS has not been characterized or qualified for use with anesthesia breathing systems with recirculation of gases.
- ONLY use a manual resuscitation bag with the GENOSYL DS for a short time (e.g., less than one hour) when on battery only. Otherwise, the System may shut off and may result in injury or death.
- ALWAYS ensure the trigger sensitivity of the ventilator is checked after connecting the GENOSYL DS to the breathing circuit. The GENOSYL DS injects and samples gas from the patient respiratory circuit which may affect the triggering sensitivity of the ventilator.
- ALWAYS ensure the patient disconnect and high-pressure alarms are used with the ventilator. Otherwise, the System is not working properly.
- ONLY use the GENOSYL DS with Bio-Med Crossvent 2+/2i+ with Constant Flow ON. Not doing so may lead to elevated NO_2 levels or dose variability.

Set-up

- ONLY VERO Biotech authorized equipment technicians are to perform the initial System set-up prior to initial use. Failure to use an authorized equipment technician can result in a patient or user injury.
- ONLY store the GENOSYL DS as outlined in the storage instructions. Not storing the device in alignment with its storage instructions can cause the device to be unsafe and lead to injury or death.
- AVOID using the GENOSYL DS adjacent to or stacked with other equipment, as it may result in improper operation. If such use is necessary, this equipment and the other equipment should be observed to verify that they are operating normally.
- DO NOT use accessories or cables other than those specified or provided by the manufacturer of this equipment, as this may result in increased electromagnetic emissions or decreased electromagnetic immunity of this equipment and result in improper operation.
- DO NOT place portable RF communications equipment (including peripherals such as antenna cables and external antennas) closer than 30cm (12 inches) to any part of the GENOSYL DS, including cables specified. Otherwise, degradation of the performance of this equipment could occur, resulting in injury.
- Only connect to a power outlet with protective earth. Failure to connect to an outlet with protective earth may result in an electrical shock.

Troubleshooting

- ALWAYS ensure patient safety before troubleshooting (such as an activated alarm) or replacing a problematic item. Not monitoring the patient prior to attending to an

alarm can result in injury or death.

Calibration

- ONLY use the calibration gas pressure regulators supplied by the manufacturer. Pressure regulators not supplied by the manufacturer may damage the sensors and may lead to patient injury.
- ALWAYS verify the correct NIST traceable calibration gas is being used and confirm the expiration date of the calibration gas prior to performing calibration. The use of incorrect or expired gas may result in inaccurate sensor readings and can lead to patient injury.

Cleaning and Maintenance

- NEVER submerge the GENOSYL DS, Cassettes, or non-disposable Adaptive Sensor Cable. Submerging in liquids will damage the System and could cause electrical shorts which may result in injury or death.

Water Trap

- ALWAYS empty Water Trap when prompted by the System, and when the trap is more than half full. Allowing the Water Trap to completely fill will occlude the Sample Line which will interrupt patient gas NO, NO_2, and O_2concentration monitoring. Failure to monitor the patient gas NO, NO_2, and O_2concentrations may result in patient injury.
- ALWAYS conduct Water Trap/ Sample Line Leak Test every time you empty and replace the Water Trap, as failure to do so may lead to an incorrect NO reading, which can result in injury or death.
- ALWAYS use a Water Trap supplied by the manufacturer. Using an incorrect Water Trap could result in non-functioning or inaccurate sensor readings.

Use Outside of Product Labeling

- ALWAYS use the GENOSYL DS in accordance with the indications, usage, contraindications, warnings, and precautions described in the GENOSYL prescribing information and labeling. Refer to latest approved prescribing information and labeling prior to use.
- The approved patient population for the GENOSYL DS as specified in the drug labeling for GENOSYL (nitric oxide) for inhalation, is limited to neonates. The GENOSYL DS is not intended to be used in other patient populations.
- ONLY use the GENOSYL DS, its parts, and accessories as instructed. Using non-specified components may result in product malfunction, injury, or death
- ONLY trained personnel should operate the GENOSYL DS. Failure to do so can result in injury or death.
- ONLY mechanical ventilators validated with the GENOSYL DS should be used. Not using a validated ventilator system can result in injury or harm.

CAUTIONS

Supplied Instructions

- ALWAYS refer to the instructions supplied with all equipment to be used in conjunction with the GENOSYL DS for their intended uses, contraindications, and potential complications. Misuse of the device or its components may damage the

device.

Cassette

- DO NOT remove Cassette from packaging until ready to use. External packaging is designed to protect the Cassette from damage and/or contamination.
- User should always have a secondary Cassette inserted in the Dosing Console and preheated in order for auto transition to occur. User should replace depleted Cassette as soon as possible after ejection.

Consoles

- ALWAYS operate the Console on a level surface to avoid potential interruption to Nitric Oxide (NO) delivery.
- ONLY use recommended cleaning agents or a damp cloth to clean the Console and limit use of liquids around Console. Excess water can permanently damage the device.
- ONLY use the GENOSYL DS with the power cord supplied by the manufacturer. Use of a generic power cord may cause output voltage instability leading to a touch screen failure.
- ALWAYS ensure the power cord is firmly seated into the power supply and the wall outlet. A loose connection can result in damage to the device or faulty operation.
- Prolonged use in dry environments without humidification will damage the gas sensors. Supplemental humidification providing greater than 20% relative humidity (RH) in the patient circuit is recommended.

Calibration

- ALWAYS perform a full-scale calibration of the GENOSYL DS when prompted by the System prior to use.
- ALWAYS confirm the correct flow direction of the installed one-way check valve in the sampling tee to avoid over pressurization of the sample System and damage to the device.

Cleaning and Maintenance

- ALWAYS follow maintenance instructions in this manual for your safety and to prevent damage to the System.
- ALWAYS power down the GENOSYL DS Console when not in use.
- DO NOT sterilize (e.g., autoclave, gas sterilize) any of the components of the System, as this may compromise performance.
- DO NOT use harsh cleaning agents. Doing so may impair the structural integrity and/or function of the device.
- DO NOT touch or rub the display screen with abrasive cleaning compounds, as they may scratch and damage the screens.
- ALWAYS ensure the System is completely dry after cleaning before powering it ON. Failure to do so could result in equipment damage.

Switching OFF the System

- NEVER turn the rear power switch OFF until the System has gone through a controlled shutdown or instructed by VERO Technical Support. Turning the rear power switch OFF prematurely (e.g., while it is still in use) will immediately shut down the device and may cause improper operation upon restart.

Cart

- DO NOT stand or sit on the Cart. Standing or sitting on the Cart can damage the device.
- ALWAYS push or pull the Cart using the handle only. NOT doing so may result in damage to the device.

TABLE OF CONTENTS

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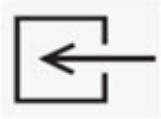
ABBREVIATIONS, TERMINOLOGY, AND DEFINITIONS

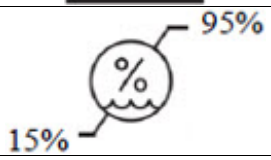
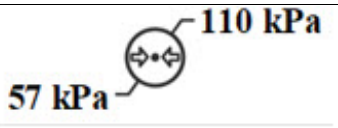
ABBREVIATION / TERMINOLOGY	DEFINITION
DS	Delivery System
Back-up	A situation whereby the Back-up Console and its Cassette is activated in the event of a failure of the Dosing Console.
Cassette	The Cassette contains the material used to make Nitric Oxide and when inserted into the Console is available for dosing the patient.
Display	Electronic information panel located on the front of the Console.
GENOSYL	Nitric Oxide for inhalation

Keypad	A Graphical User Interface function built into the Console display and used to enter the Nitric Oxide dose to be administered to the patient.
L/min	Liters per minute
LPM	
Mixer	Ventilator circuit accessory used to mix the ventilator gas with the gas supplied by the GENOSYL DS for specific ventilator and tidal volume use cases, per Section 10.2.
MRI	Magnetic Resonance Imaging
MR Scanner Bore	The MR scanner opening
MR Exclusion Zone	Area in the MR scanner room where the magnetic field is greater than 100 gauss
MR Scanner	The MR device for diagnostic imaging
MR Scanner Room	The room where the MR scanner is located
NICU	Neonatal Intensive Care Unit
NO	Nitric Oxide
NO Injection Port	Port on the front of the Console that introduces the concentrated NO into the respiratory circuit.
Adaptive Sensor Port	Port on the front on the Console that the Adaptive Sensor Cable plugs into.
Gas Sample Port	Port on the front of the Console at the Water Trap that measures NO, NO_2 and O_2 levels within the NO gas path prior to reaching the patient.
NO_2	Nitrogen Dioxide
O_2	Oxygen
ppm	Parts Per Million
Dosing Console	The Console that is actively dosing NO.
Back-up Console	The secondary Console used as a "Back-up" system to administer Nitric Oxide when the Dosing Console cannot be used.
System	The System (GENOSYL DS) consists of a Cart with two Consoles, Cassettes, and component parts used to set up the gas lines
v	Electrical Volts

SYMBOLS

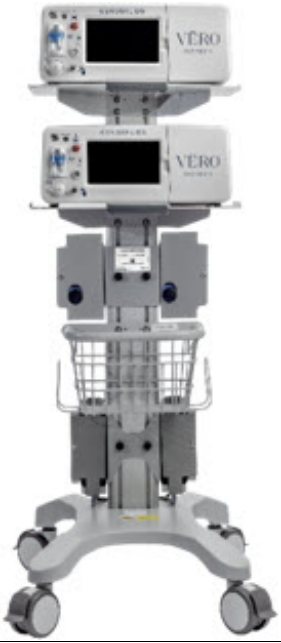
Symbol	Symbol Name	Description
	Magnetic Resonance (MR) Conditional	Indicates that the System has been demonstrated to pose no known hazards in a specified MRI environment with specified conditions of use.
	Magnetic Resonance (MR) unsafe	Keep away from magnetic resonance imaging equipment.

	RF Interference	Devices marked with this symbol may interfere with the Console.
	Water Trap Attachment Point	Indicates the location where the Water Trap with Sample Port is to be attached.
	Unlock position	Direction to push to open the Water Trap.
	Sample Gas Inlet	Attachment point for Sample Line on Water Trap
	NO Injection	Output port for GENOSYL to patient circuit
	Calibration Port	Input port for calibration gas
	Adaptive Sensor Port	Input port for Adaptive Sensor Cable
	Manual Ventilation	Output port for GENOSYL to manual ventilation system
	Operating Instructions	Refer to operating instructions for instructions for use, warnings, precautions, and other equipment information.
	AC	Indicates power input specification is alternating current (AC).
IPX1	Ingression	Code for the level of ingression protection tested. The enclosure was tested to be drip proof.
	Catalog or model number	Indicates the catalog number so that the medical device can be identified.
	Batch Code	Indicates the batch code so that the batch or lot can be identified.
	Serial Number	Indicates the serial number so that a specific medical device can be identified.
	Date of Manufacture	Indicates the date when the medical device was manufactured.

	Manufacturer	Indicates the manufacturer of the item.
	Storage humidity range	Indicates the range of humidity to which the medical device can be safely exposed.
	Storage temperature range	Indicates the temperature limits to which the medical device can be safely exposed.
	Atmospheric pressure limitation	To indicate the acceptable upper and lower limits of atmospheric pressure for transport and storage.
	Do not reuse	Indicates a medical device that is intended for one use, or for use on a single patient during a single procedure.
	Attention	Indicates the need for the user to consult the instructions for use for important cautionary information such as warnings and precautions that cannot, for a variety of reasons, be presented on the medical device itself.
	Use by	Indicates the date after which the medical device is not to be used.

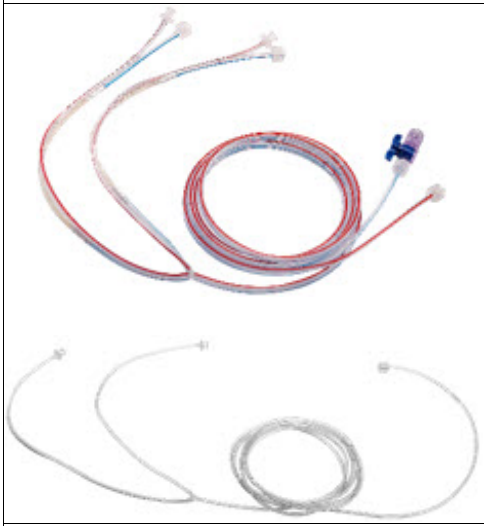
GENOSYL DS PARTS / COMPONENTS

PART	PART NAME	VERO BIOTECH PART NUMBER
	**GENOSYL DS Console** (2 required per System)	602166

	**MR Conditional GENOSYL DS System**	GENOSYL DS Console (2) 602166 GENOSYL DS Cart 602524 Gauss Alarms Mount (2 gauss alarms installed) 601823
	**GENOSYL DS Cart**	602524
	**Gauss Alarms Mount** (2 gauss alarms installed)	601823
	**Adaptive Sensor Cable**	602489

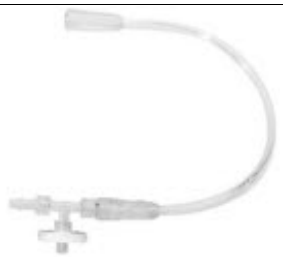
The following parts are required to set up the GENOSYL DS and deliver Nitric Oxide to the patient breathing circuit, using validated ventilators, ventilator circuits, and manual ventilation equipment.

PART	PART NAME	VERO BIOTECH PART NUMBER

	**GENOSYL Cassette**	601772
	**Adaptive Sensor**	602490
	**NO Gas Injection Adapter** 22M/15F × 22F	601503
	**Adapter** 22F × 22F	601473
	**Inline Breathing Circuit Filter**	5003-0015
	**GENOSYL DS Mixer**	601445
	**GENOSYL DS Gas Lines:** NO Injection Line (red) Sample Line (blue) Manual Ventilation Line (clear)	601690

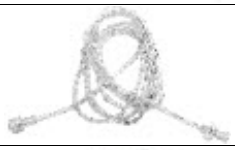
	**GENOSYL DS Sample Line Extension**	601955
	**Neonatal Gas Sample Tee**	601474
	**Water Trap**	600896
	**22M 22F Elbow Adapter**	601746
	**Sample Tee, 3/8" Barbed**	601970
	**Injection Line Filter**	601758

The following parts are required to deliver Nitric Oxide using a manual ventilation system.

PART	PART NAME	VERO BIOTECH PART NUMBER
	**GENOSYL DS Manual Ventilation Bag NO Adapter**	601485

The following parts are required for routine maintenance.

PART		VERO BIOTECH PART NUMBER
	**Calibration Gas - 45 ppm NO**	601856

	**Calibration Gas - 10 ppm NO_2**	601857
	**Calibration Regulator**	601860
	**Calibration Tee Tubing**	601861
	**Calibration Extension Tubing**	G01436
	**Calibration Gas Carrying Case**	601859
	**Calibration Equipment Wrench**	601862

SECTION 1
GENERAL INFORMATION

1. GENERAL INFORMATION

1.1 User Responsibility

The GENOSYL DS (Console) will perform as described in this Operator's Manual, accompanying inserts, and/or labels when assembled, operated, maintained, and repaired in accordance with the instructions provided. The Console must be set up as described in Section 3. If the Console does not perform as described in Section 3 or during assembly, the parts are found to be broken, missing, contaminated, or visibly worn, they should be replaced immediately.

In the case of repair or replacement of the Console is required, a telephone service request should be made to **Technical Support at 877-337-4118.**The GENOSYL DS or any of its parts should not be serviced or repaired by anyone other than a VERO Biotech Technical Engineer or without written permission from VERO Biotech Technical Engineering Department.

Any malfunction resulting from faulty maintenance, improper repair, damage, alteration by anyone other than a VERO Biotech Technical Engineer, and/or improper use will be the sole responsibility of the User.

WARNING
The GENOSYL DS must only be used in accordance with the approved indications, usage, contraindications, precautions, and warning described in the GENOSYL DS labeling. Refer to the labeling prior to use.

CAUTION
U.S. Federal law restricts this device to sale by or on the order of a physician. Outside the U.S., check local laws for any restrictions that may apply.

NOTES
• Prior to using the GENOSYL DS, read through this Operator's Manual. • Follow all instructions and obey the Warnings and Cautions. • Keep this Operator's Manual available to readily answer questions. • Read through all manufacturer Operator's Manuals for the ventilator, humidifier and any other accessory items used.

1.2 General Information and Indications for Use

GENOSYL DS generates and delivers NO for inhalation at the point of use. The concentration of NO, as set by the user, is monitored, and adjusted to accurately dose the patient throughout an inspired breath. Only validated devices / components should be used with the GENOSYL DS.

The intended population for inhaled NO treatment is term and near-term neonates in neonatal intensive care units (NICUs). Refer to the GENOSYL (nitric oxide) for inhalation drug label for more detailed information.

The GENOSYL DS is intended for use in the hospital and 1.5 Tesla and 3.0 Tesla diagnostic imaging environments.

The GENOSYL DS is intended for use by healthcare professionals (HCPs) who are licensed and actively practicing pediatric and/or neonatal respiratory therapists (RTs) in the United States. These users are required to set up, administer inhaled Nitric Oxide and provide respiratory care (including initiation and maintenance of mechanical ventilators) in the critically ill neonatal population.

The GENOSYL DS starts with liquid N_2O_4/NO_2, which is then converted in a proprietary Cassette to NO. The GENOSYL DS delivers NO into the ventilator stream, where the NO joins a stream of air or $O_2$and is diluted to the prescribed concentration.

The NO concentration (dose) to be delivered to the patient is selected by the user and is set and maintained independently by means of computer-controlled air pumps, Cassette heaters, and a feedback loop that measures the delivered NO concentration.

The GENOSYL DS takes a gas sample removed from the NO gas flow stream

immediately prior to the patient and provides real-time output of the NO, NO_2, and O_2 concentrations that are being delivered to the patient. The continuous integrated gas monitoring includes a comprehensive alarm system.

The NO concentration detected from the sample line is used in a feedback loop to adjust the NO concentration delivered into the ventilator circuit.

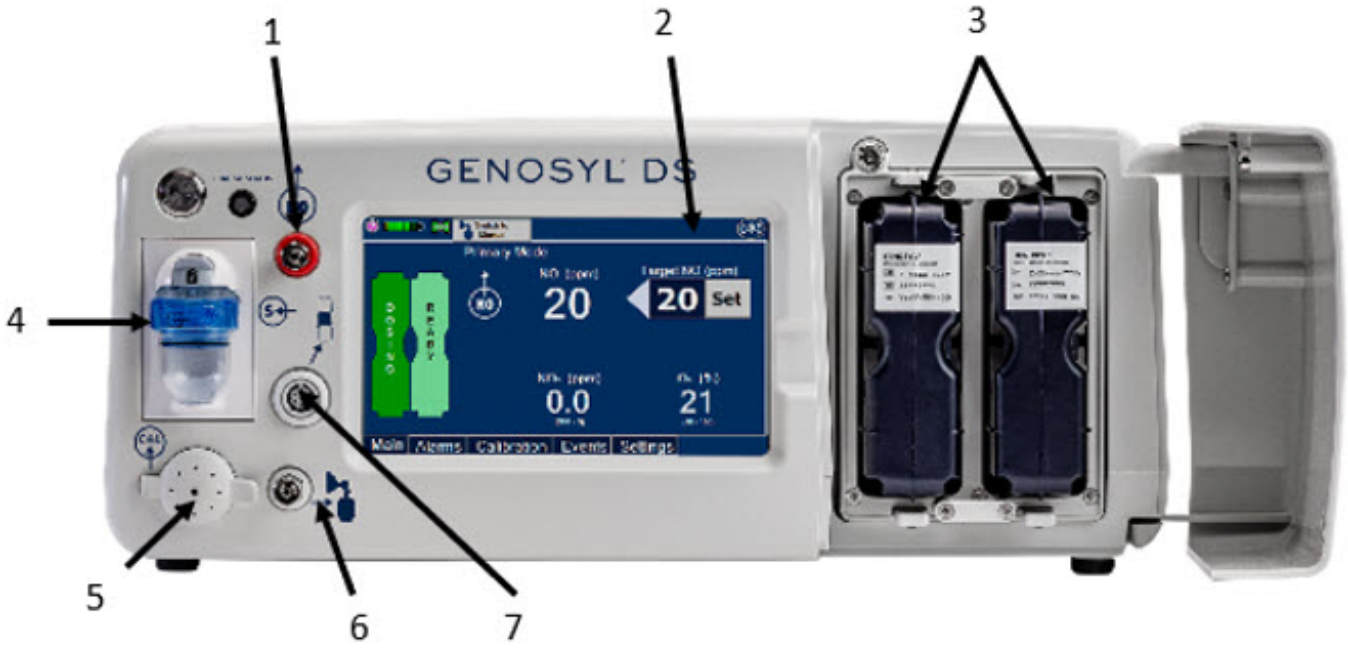
The GENOSYL DS includes a redundant Console for complete Back-up capability for delivery of NO for inhalation. Each Console has a back-up battery that provides at least 1 hour of NO delivery in the absence of an external power source.

1.3 Principles of Operation

GENOSYL DS. The GENOSYL DS continuously introduces a precisely controlled concentration of Nitric Oxide (NO) into the inspiratory limb of the ventilator circuit. GENOSYL DS utilizes the known properties of NO and other oxides of nitrogen, namely dinitrogen tetroxide (N_2O_4) and nitrogen dioxide (NO_2), to create a "tankless" drug/device combination System to produce, at the point of use, ultra-high purity NO for inhalation, providing a consistent, prescribed dose to the patient.

Console. The GENOSYL DS Console contains the electronics to control the production and to maintain the constant and precise delivery of NO.

The primary features of the Console front panel are displayed in Figure 1.



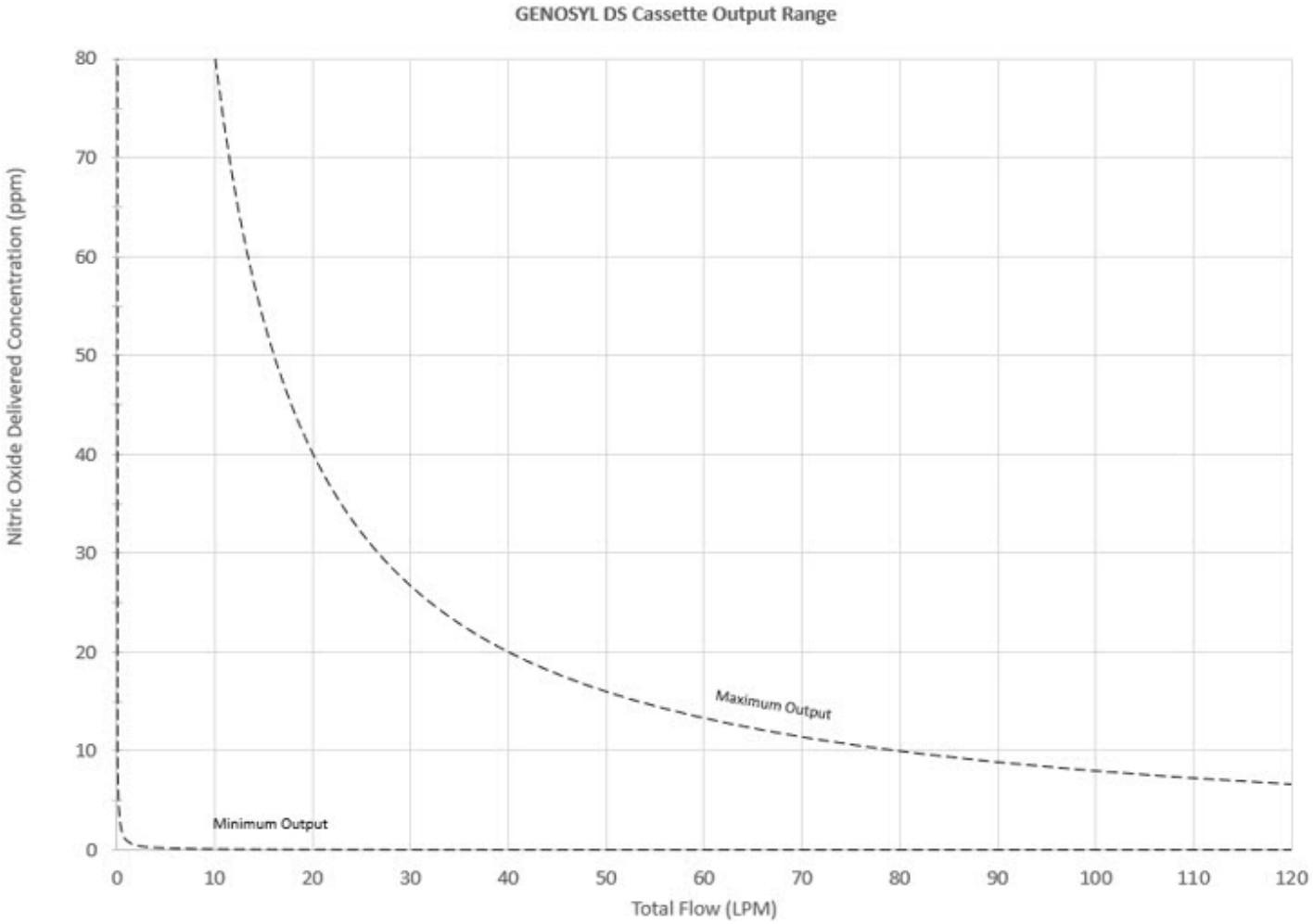
1. NO Gas Delivery Port
2. Interactive Touch Screens and Alarms
3. Dual Cassette Receptacles
4. Gas Sampling Port with Water Trap
5. Gas Sensor Calibration Port
6. Manual Ventilation Port
7. Adaptive Sensor Port

NO generation. The Console uses Cassettes containing liquid N_2O_4/NO_2 inside a stainless-steel vessel (the liquid module) and an antioxidant cartridge. Upon initiation of a Cassette, the liquid N_2O_4 is heated, producing NO_2 gas, which is mixed with up to 0.9

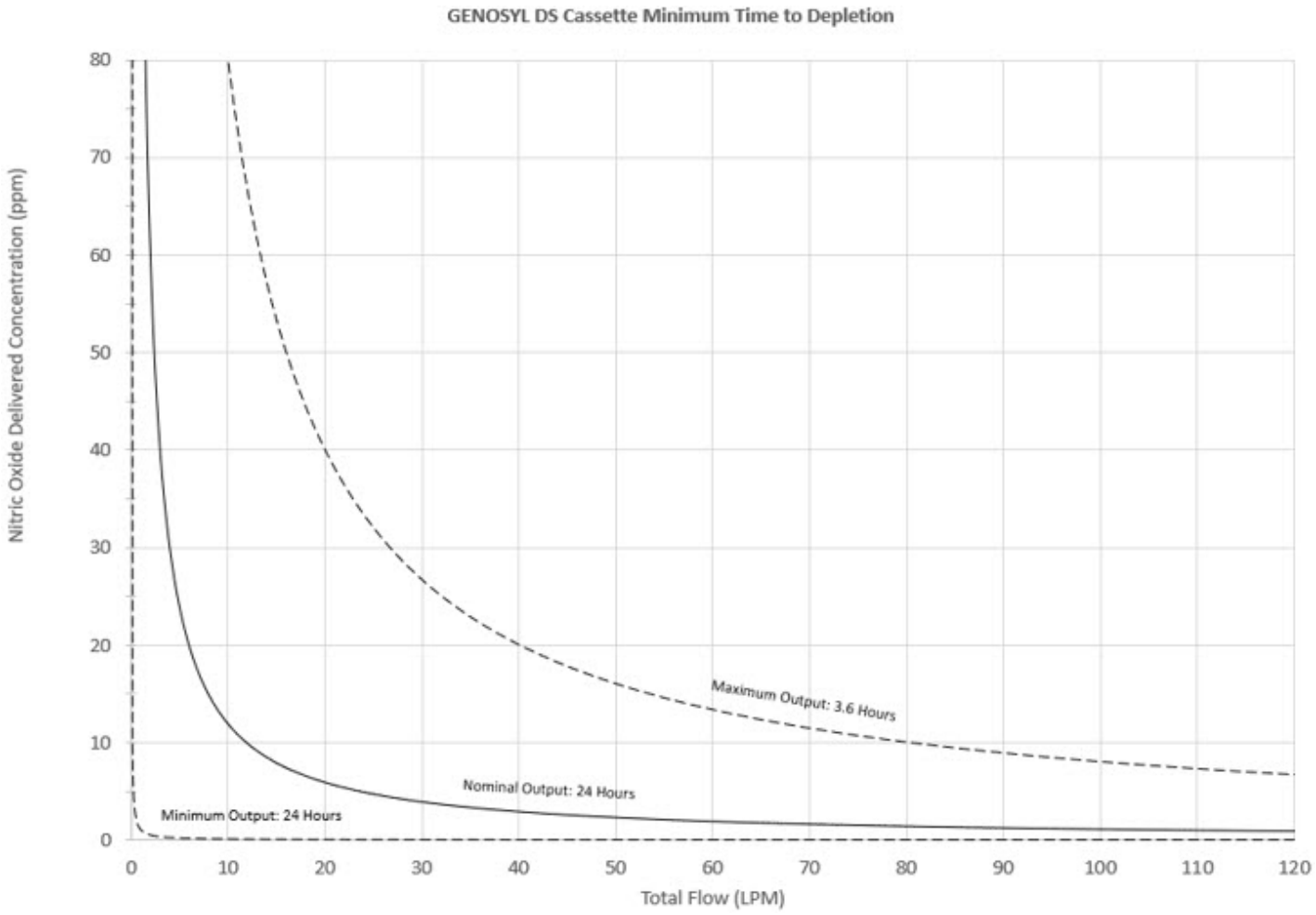
LPM ambient air supplied by the Console. The NO_2/air is injected into the antioxidant cartridge inside the Cassette, which converts NO_2 to NO.

The Cassette is designed to provide NO in concentrations up to 80 ppm. The maximum and minimum delivered dose for a range of constant inspiratory flow rates is presented in Figure 2.

The maximum combination of dose (ppm) and flow (LPM) output of the System is 800 ppm × LPM (e.g., 20 ppm with 40 LPM, 40 ppm at 20 LPM, etc.). The System is capable of delivering NO at a minimum of 1 ppm × LPM (e.g., 1 ppm at 1 LPM).



The total time to deplete the Cassette N_2O_4 contents depends on the rate of use. The minimum time to depletion based on use rate is shown in Figure 3. The calculated minimum remaining contents at the current output rate is indicated by a gauge presented on the Console display during use.



NO Injection into the Ventilator Circuit. After NO is produced in the Cassette, the NO injector introduces the concentrated NO into the ventilator circuit where the NO is diluted to the prescribed concentration (dose) and mixed with the O_2 or air supplied to the patient.

Before the gas mixture reaches the patient, a sample line removes a small gas sample and sends it back to the Console, where gas sensors continuously measure the supplied NO, NO_2 and O_2. The Console software then compares the measured NO concentration to the set NO concentration and continuously adjusts the delivery of NO to maintain the prescribed NO concentration (dose) delivered to the patient (closed loop control). The Console software commands the NO injection flow rate into the ventilator circuit with a maximum flow rate of 0.9 LPM. Changes in the ventilator settings by the user may cause brief transient changes in the measured NO value. The Console software will adjust the injected flow rate and the internal temperature of the Cassette to compensate for the changes in the total ventilator flow rate. For example, a higher minute ventilation will require a higher injection flow rate to produce the same NO concentration.

Mixer. An inline Mixer is used in the applicable ventilator circuit after the NO injection site and before the gas sample site to mix NO from the Console with the gas supplied by the ventilator, for specific ventilator and tidal volume use cases per Section 10.2.

Gas Monitoring.The gas mixture delivered to the patient by the GENOSYL DS is continuously monitored with two NO detectors, with one providing redundant back-up, as well as a detector for NO_2 and O_2. A sample of inspired gas is taken from the

inspiratory limb, close to the patient, and is measured by the gas sensor within the Console. The gas monitoring sensors are electrochemical; they are specific to each gas and provide an electronic signal that is proportional to the concentration of gas present.

Adaptive Sensor. The Adaptive Sensor is used to detect flow in the patient breathing circuit. When flow is not detected by the Adaptive Sensor, Nitric Oxide delivery will be interrupted until flow is detected. The Console will provide a visual and audible high priority alarm when flow is not detected to alert the user (see Section 8.2). Once flow is detected, the Console will auto resume delivery of nitric oxide at the previously set dose. An Adaptive Sensor is recommended for use with certain breathing devices. Refer to Section 3 for recommended set up diagrams. The GENOSYL DS will properly deliver and control Nitric Oxide dose in the absence of an Adaptive Sensor.

Alarms and Dosing Safeguard Fallback Modes. The GENOSYL DS alerts the user in the event of excursions of NO, NO_2, and Oxygen from their expected ranges. Nitric Oxide delivery interruption conditions are as follows:

1. NO > 100 ppm
2. NO_2 reaches 3 ppm
3. The measured respiratory circuit dilution flow drops below 0.3 SLPM as measured by the Adaptive Sensor.

The Console will provide a visual and audible high priority alarm. When detecting a sustained gas level higher than the above limits for 11 consecutive seconds, the Console will interrupt delivery of NO until the sampled levels of NO and/or NO_2 decrease to a safe level. Once sampled levels are in acceptable range, the Console will resume delivery with previously set dose.

If the cause of the high gas cannot be resolved, the use of the Back-up Console may be required. Refer to Section 8.1 for additional information on alarms and dosing safeguards.

If NO delivery was interrupted due to the GENOSYL DS Adaptive Sensor reading dropping below 0.3 SLPM, the Console will resume delivery with the previously set dose once the Adaptive Sensor reading exceeds 0.35 SLPM. The automatic resumption of dose delivery after the interruption conditions listed above are cleared is one of the safety fallback modes of the GENOSYL DS.

Back-up NO Delivery. The Back-up Console is used to administer Nitric Oxide when the Dosing Console cannot be used. This Console has a separate power supply, and at least one Cassette loaded and preheated. If the Dosing Console fails to deliver NO, the Back-up Console is ready to begin dosing to continue NO delivery.

Transition to a new Cassette. When a Cassette approaches depletion, the Dosing Console will automatically transition to the second Cassette in the Console. Once the dosing Cassette is depleted, the Dosing Console will eject the depleted Cassette and alert the user to replace via the Cassette Status Indicator.

Disposal of the Cassette. Following use, any remaining Cassette contents are purged into an inerting chamber, where the contents are chemically neutralized, rendering the Cassette safe for disposal.

1.4 Exposure of Healthcare Providers to NO and NO_2

Occupational exposure of healthcare providers to NO or NO_2 may occur during Inhaled

NO therapy for patients. Below are examples of calculated and observed exposure to NO or NO_2, in the context of guideline workplace exposure limits.

Calculated and observational methods show that the exposure levels to NO or NO_2 from an NO delivery System are significantly less than the levels recommended by the National Institute for Occupational Safety and Health (NIOSH).

Workplace Limits: NIOSH has recommended workplace exposure limits as follows [1].

NO	time-weighted (8 hours) average concentration limit of 25 ppm
NO_2	Recommended exposure limit of 1 ppm

Theoretical Calculation. The build-up of NO in a well-ventilated ICU room, with NO flowing directly into the room, can be evaluated using the following calculation:

Room size	1000 ft^3
Room volume	28,300 L
Room ventilation (6 complete exchanges/hour)	2,830 L/min
NO flow into the room	80 ppm at 14 L/min
Average NO room concentration (80 × 14) ÷ 2,830 = 0.396 ppm (0.4 ppm)	0.4 ppm of NO

***Observations of NO Exposure*.** The theoretical calculation has been supplemented by actual measurements in three independent studies in actual therapeutic use settings. [2,3,4] The studies found that detectable exposures to NO and NO_2 were brief, infrequent, and well below recommended exposure limits.

If the location for using NO has uncertain ventilation, then the location should be evaluated for NO and NO_2 build-up prior to use.

GENOSYL ®DS

SECTION 2
SYSTEM OVERVIEW

2. SYSTEM OVERVIEW

2.1 Frequently Used Functions

Detailed instructions are provided in this manual for the primary user interaction and frequently used functions of the GENOSYL DS, which include:

System Set-Up and Connections (Section 3 **)**

- Connections to Various Breathing Systems
- GENOSYL DS Ventilator Circuit Assembly Pre-Check
- GENOSYL DS Injection Assembly with Adaptive Sensor
- GENOSYL DS Mixer Assembly with Adaptive Sensor
- GENOSYL DS Console Connections
- GENOSYL DS Gas Line Connections
- GENOSYL DS Sample Line Extension Connection

- GENOSYL DS Adaptive Sensor Cable Connection
- GENOSYL DS Ventilator Circuit Connection
- GENOSYL DS Manual Ventilation Connections
- GENOSYL DS Mechanical Ventilator Circuit Connections

System Start-Up (Section 4 **)**
- Console Start-Up
- Cassette Insertion
- Water Trap / Sample Line Leak Test

Nitric Oxide Administration (Section 5 **)**
- Setting a Dose when using a Circuit with an Adaptive Sensor
- Setting a Dose when using a Circuit without an Adaptive Sensor
- Adjusting the Dose
- Manual Mode
  - Manual Ventilation Use (Bagging)
  - Preset Manual Mode Flow Rate (Optional0
  - Resuming Primary Dosing
- Console Use as Back-up

Console Shutdown (Section 6 **)**
- Console Shutdown
- Cassette Removal
- Cassette Disposal

Using the System in the MR Scanner Room (Section 7 **)**
- Connection to the Ventilator Circuit
- Transferring to and from the MR Scanner Room

Alarms, Alerts, and Troubleshooting (Section 8 **)**
- Alarms (High, Medium, and Low Priority)
- Informational messages
- Troubleshooting

System Maintenance (Section 9 **)**
- Calibration
- Maintenance Schedule
- Testing the GaussAlert™ Function
- Water Trap Maintenance
- Battery
- Cleaning
- Storage

2.2 GENOSYL DS Cart and Consoles

The following pages contain photos of the GENOSYL DS Consoles. The specific sections of the GENOSYL DS are numbered with the respective description listed below the photo.

WARNING

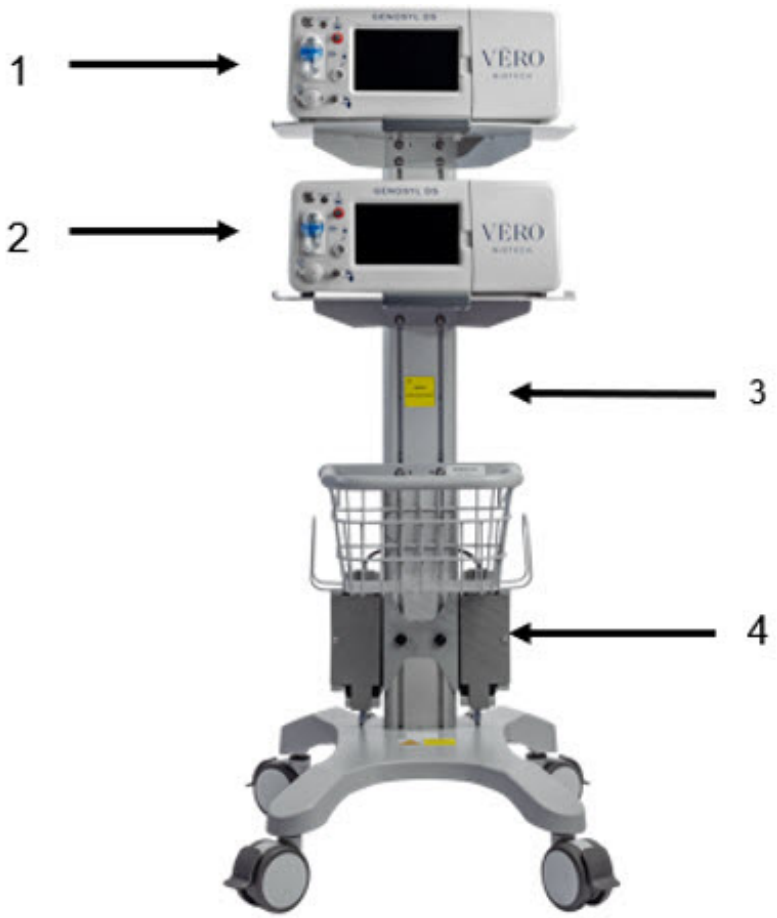
- NEVER use the MR Unsafe GENOSYL DS Cart in the MR scanner room.
- ALWAYS verify at least one gauss alarm is functioning properly prior to use in the MR environment.

CAUTION

- ALWAYS operate the Console on a level surface to avoid potential interruption to Nitric Oxide (NO) delivery.
- DO NOT stand or sit on the Cart. Standing or sitting on the Cart can damage device.
- ALWAYS push or pull the Cart using the handle only. NOT doing so may result in damage to the device.

NOTE

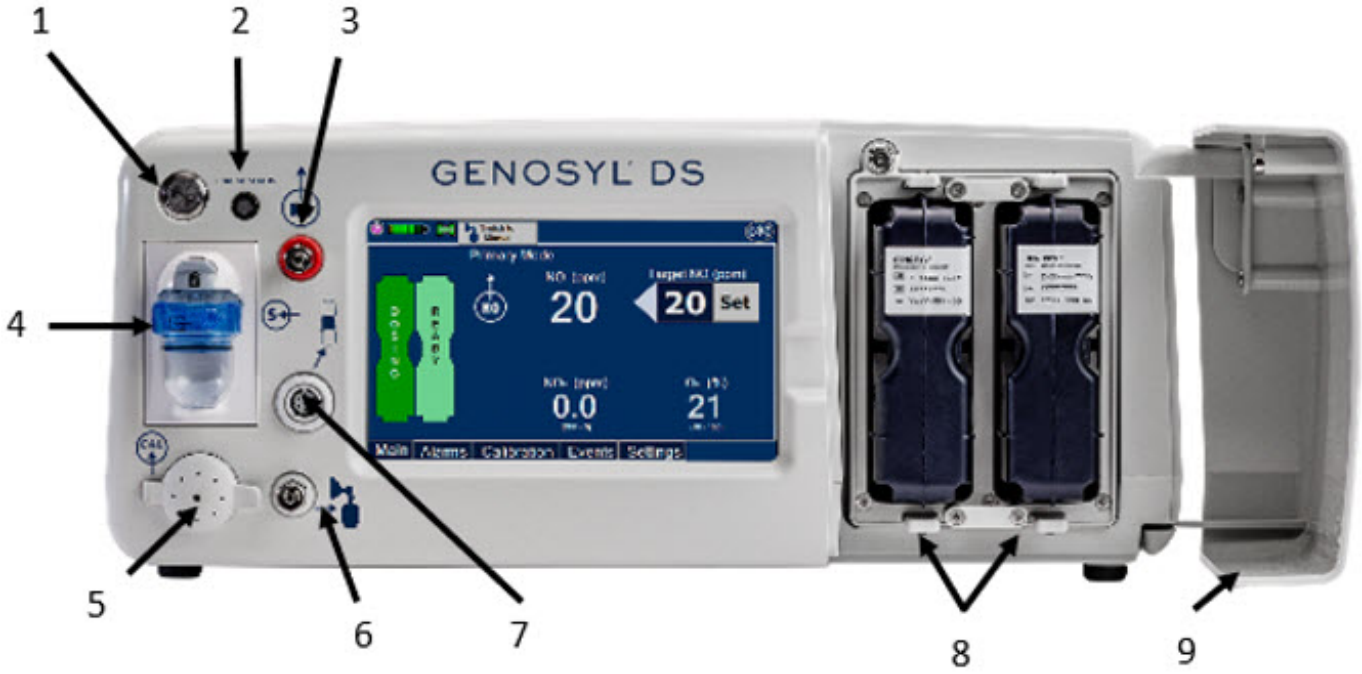
A System has a top and bottom Console. Both Consoles will start-up in Primary Mode. One Console will be used for dosing and the other will remain in Primary Mode as a Back-up Console. (See Section 5.5)



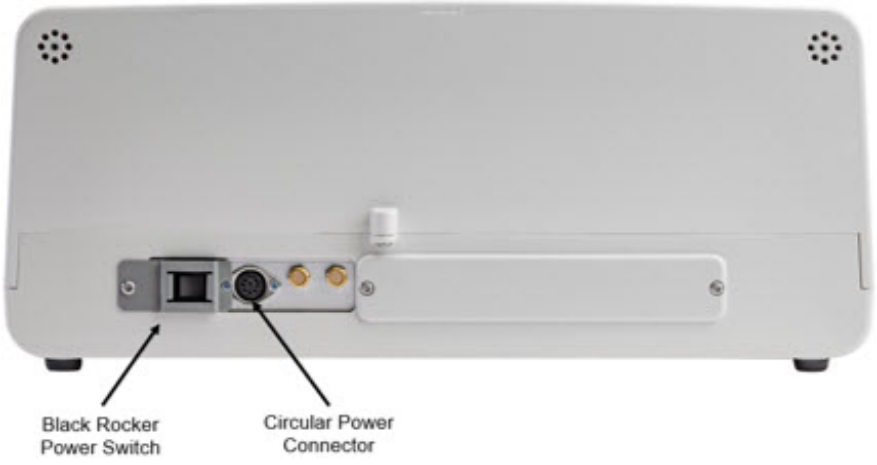
1. Top Console
2. Bottom Console
3. Cart
4. Power Supplies

1. Gauss Alarm Mount (two gauss alarms installed
2. Locking Casters
3. Gauss Alarm
4. Battery Indicator
5. Alarm Volume Adjustment

1. Optional Tether Point
2. Gauss Alarms Mount (two gauss alarms installed)
3. Gauss Alarm



1. Silver Power Button
2. Battery Charge Indicator
3. NO Delivery Port
4. Water Trap with Gas Sample Port
5. Calibration Port
6. Manual Ventilation Port
7. Adaptive Sensor Port
8. Dual Cassettes
9. Cassette Access Door



2.3 Cassette

The Cassette contains the material that will be converted to nitric oxide during the activation process. It is inserted into the GENOSYL DS Console, and its shape helps ensure proper orientation during the insertion process. A Cassette State Window is located on the front of the Cassette to indicate if the Cassette is available for use (blue), or if it has been inerted and unavailable for use (bleached and reddened).

Cassette in Packaging 
Unused Cassette

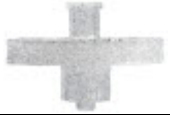
Inerted Cassette

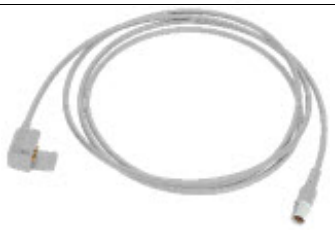
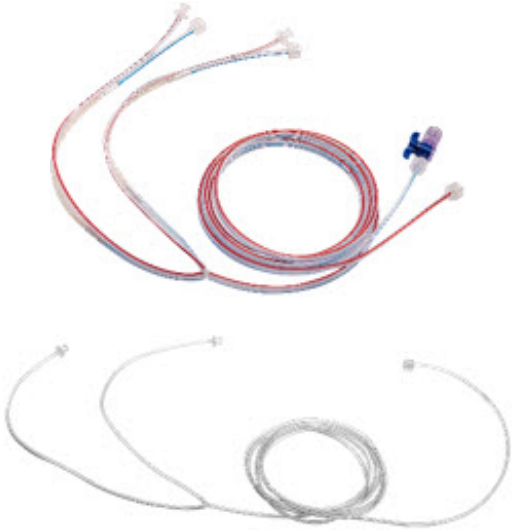
Figure 11: GENOSYL Cassette

CAUTION
DO NOT remove Cassette from packaging until ready to use. External packaging is designed to protect the Cassette from damage and/or contamination.

2.4 GENOSYL DS Ventilator Circuit Components

The following parts are used to set up the GENOSYL DS portion of the patient respiratory circuit, as specified in Section 3.2.

PART	PART NAME	FUNCTION
	**NO Gas Injection Adapter** 22M/15F × 22F	Used between the Adapter and the Mechanical Ventilator Inspiratory Outlet, and to connect to the NO Injection Line (red).
	**Injection Line Filter**	Used to filter air from the Injection Line.

	**Adaptive Sensor**	Used to measure flow from the ventilator into the circuit.
	**Adaptive Sensor Cable**	Used to communicate flow readings to the Console.
	**GENOSYL DS Gas Lines** NO Injection Line (red) Sample Line (blue) NO Manual Ventilation Line (clear)	Used to deliver Nitric Oxide to the ventilator circuit and manual ventilation bag, and to sample gas within the ventilator circuit.
	**GENOSYL DS Sample Line Extension**	Used when the distance between the patient and the DS exceeds the length of the standard sample gas line in the MR Environment.
	**Neonatal Gas Sample Tee**	Used to connect the Sample Line to the ventilator circuit.
	**GENOSYL DS Mixer**	Used to mix the NO gas with the gas supplied by the ventilator through a filter containing silica gel to provide intra-breath NO delivery for certain scenarios.
	**Adapter** 22F × 22F	Used as a coupler between the Mixer and the Gas Injection Adapter when a mixer is required.
	**Inline Breathing Circuit Filter**	Used to filter air from the Injection Line.

	**Sample Tee, 3/8" Barbed**	Used to accommodate gas sampling in some ventilator circuits, (e.g., Crossvent Infant Circuit).
	**GENOSYL DS Manual Ventilation Bag NO Adapter**	Used to connect oxygen tubing to manual ventilation bagging system to deliver nitric oxide. Includes an NO Injection Port to connect to the NO Injection Line.
	**Water Trap**	Used to protect sample system by collecting condensation and filtering contaminants from the sampled gas. The Water Trap may need to be emptied or changed while in use (refer to Section 9.4).

2.5 Gas Lines (detailed explanation)

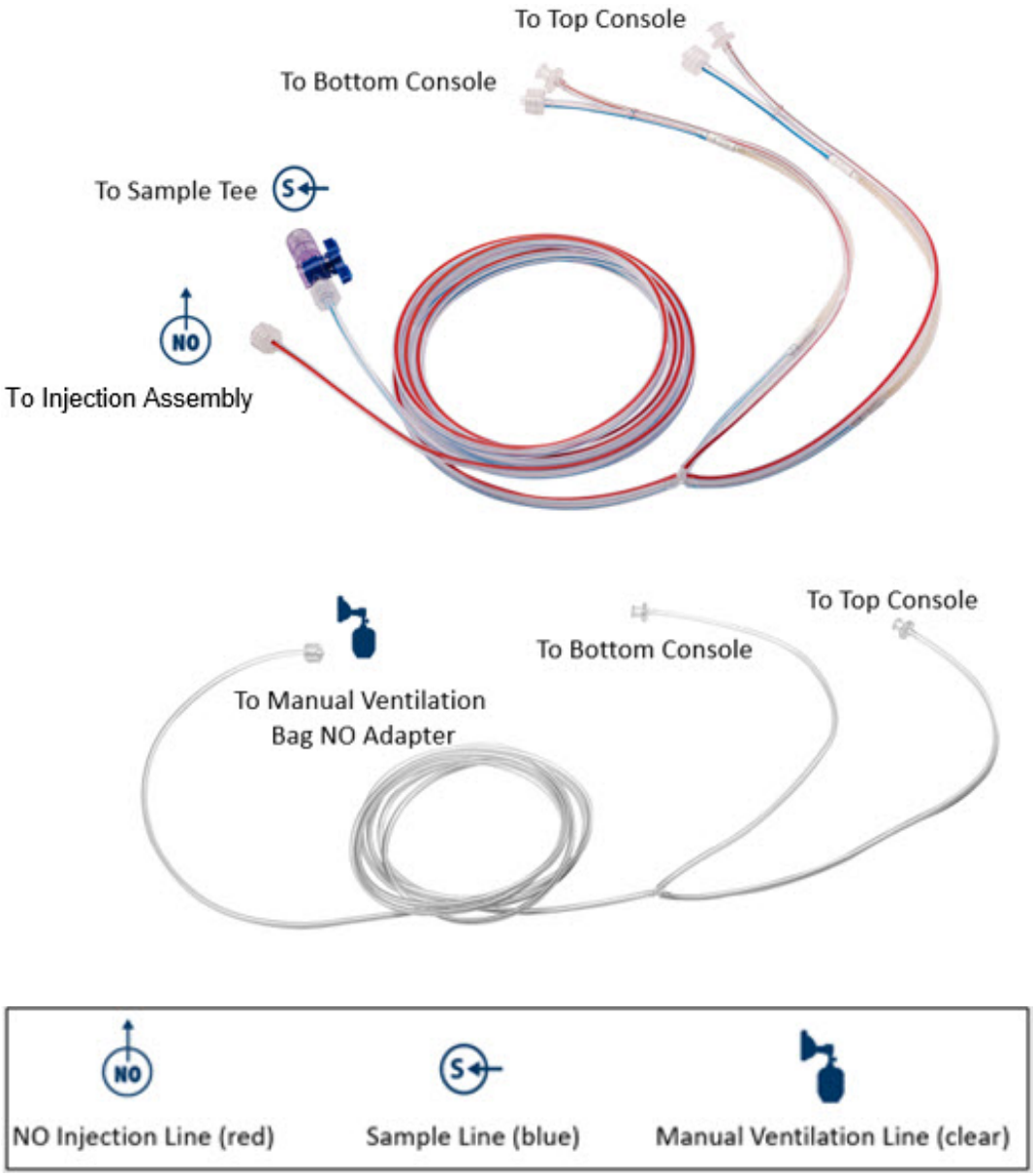
Gas lines are used to deliver nitric oxide from the GENOSYL DS Consoles to the ventilator circuit and manual ventilation bag, and to sample gas within the ventilator circuit. The lines are color coded and labeled with icons corresponding to colors and icons on each Console.

The NO Injection Line (red) delivers Nitric Oxide from the Console to the mechanical ventilation circuit (described in Section 3.5).

The Sample Line (blue) also contains a stopcock to conduct the Water Trap / Sample Line Leak Test (described in Section 4.2).

A Sample Line Extension is available when additional distance between the patient circuit and the Console is required (e.g., use in the MR environment) (described in Section 3.5.2).

The Manual Ventilation Line (clear) delivers Nitric Oxide from the Console to the Manual Ventilation Bag NO adapter (described in Section 3. 6).



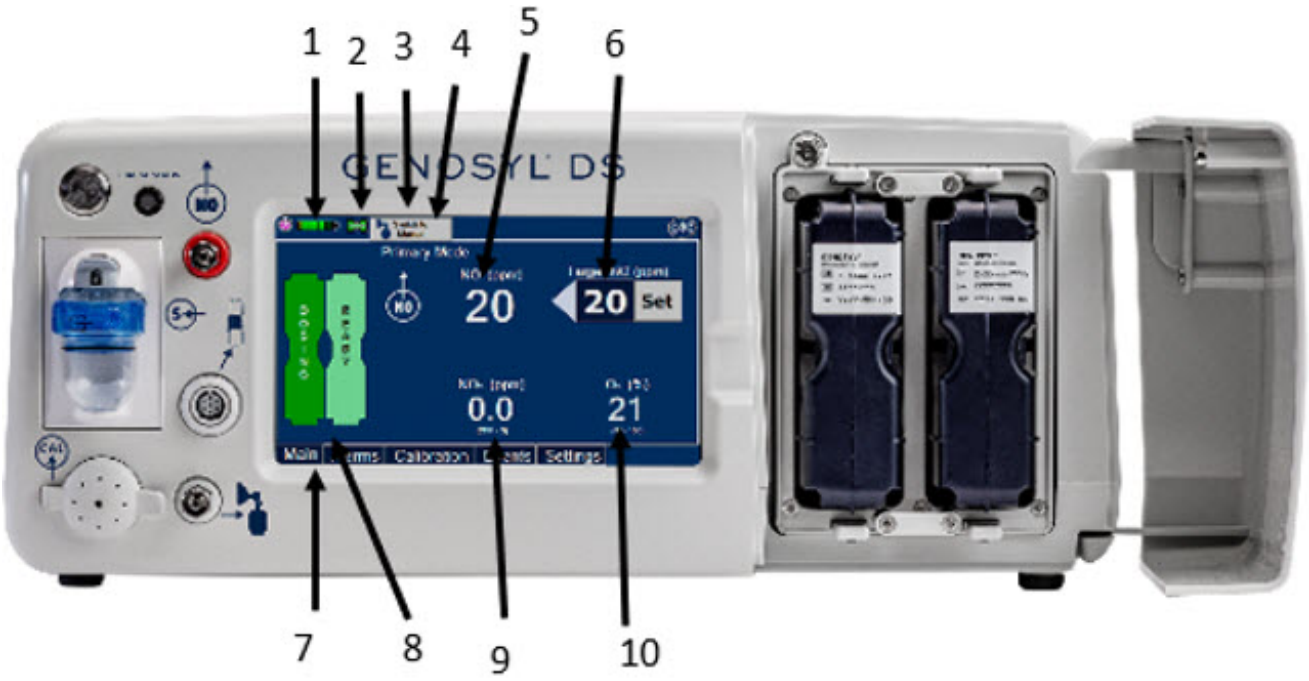
2.6 Console Modes of Operation

During operation, a Console can be in one of two modes; **Primary**or **Manual**. The user can switch the modes during normal operation to perform specific functions for certain conditions. The following table summarizes key characteristics of each mode.

MODE	FUNCTIONAL CHARACTERISTICS
Primary	• The mode of operation for controlled dosing with Smart Feedback System™.
Manual	• The mode of operation used for manual ventilation. • Manually adjustable fixed dosing without the need of feedback for certain conditions.

2.7 Display Screen

The GENOSYL DS display screen is presented below (Figure 13) followed by a table with descriptive text corresponding to the numbers shown around the display screen.



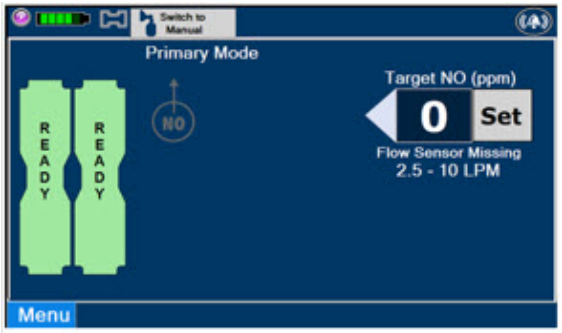
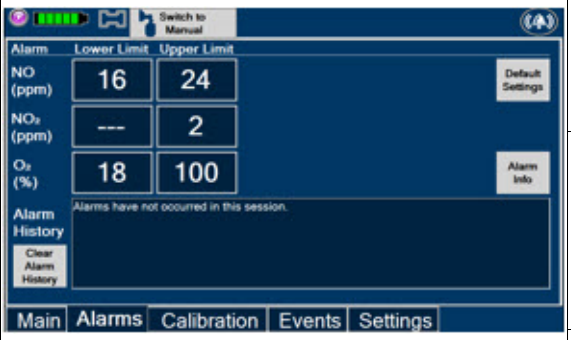
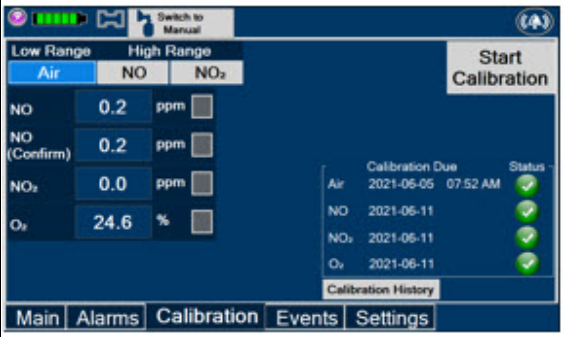
1. Battery Charge Status Indicator
2. Adaptive Sensor Indicator
3. Mode Switch Button
4. Console Mode
5. Measured NO Dose (ppm)
6. Target NO Dose (ppm)
7. Menu Tab
8. Dual Cassette Status Indicator
9. NO_2 Measured Level (ppm)
10. O_2 Measured Level (ppm)

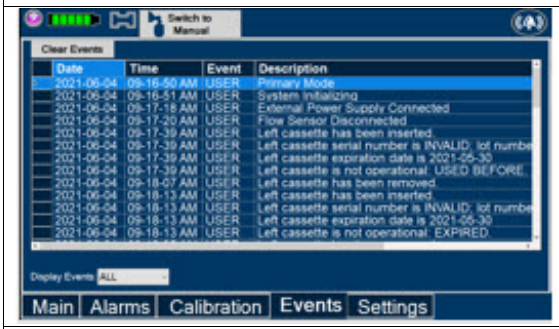
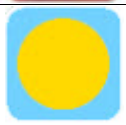
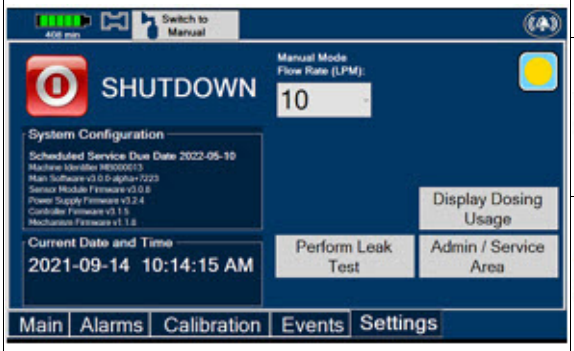
NOTE
Some confirmation display screens (e.g., "Confirm", "Yes", "Accept", etc.) will be semi-transparent after dosing has been initiated to allow the Operator to continue to see important information on the underlying screen (e.g., NO values, Alarms, Alerts, etc.).

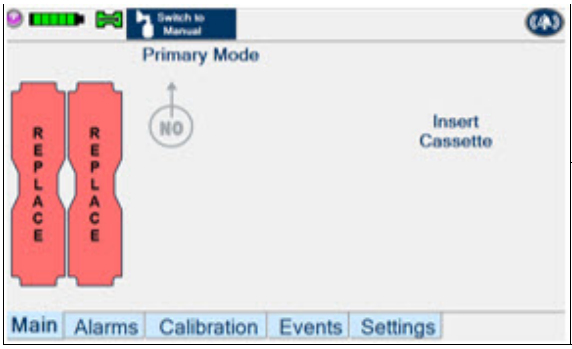
2.8 Display Menu Tab Navigation

The table below consists of the available Menu tabs (Main, Alarms, Calibration, Events, and Settings) along with the functional description of each tab, and the buttons within each tab.

MENU TAB DISPLAY	TAB / BUTTON	DESCRIPTION

	Menu	Press this tab to access the sub-level tabs (Main, Alarms, Calibration, Events, and Settings).
	Alarms	Displayed when the Alarms Tab is selected, this screen is used to set the Upper and Lower Alarm Limits for NO (ppm), NO $_2$(ppm), and O $_2$(%). A list of Alarms that have occurred since the last reset for the Console will be displayed on this tab.
		NOTE See Section 8for additional information on alarms and alerts.
	Default Settings	Displayed after pressing the Alarms tab, press this button to switch to the default upper and lower limits for NO (ppm), NO $_2$(ppm), and O $_2$(%).
	Clear Alarm History	Pressing this button will clear the alarm history from the alarm log visible on this tab. The alarm will remain logged in the Console's permanent logs.
	Main	Press this tab to return to the main screen. Pressing the Main Tab will collapse the tab menu.
	Calibration	Press this tab to access the calibration screen.
		NOTE See Section 9.1for additional information on Calibration.
	Air	Press this button to calibrate the low range of the NO and NO $_2$sensor.
	NO	Press this button to calibrate the high range for the NO sensor.
	NO₂	Press this button to calibrate the high range for the NO $_2$sensor.
	Start Calibration	Press this button to initiate calibration for the selected gas.

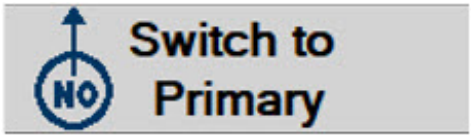
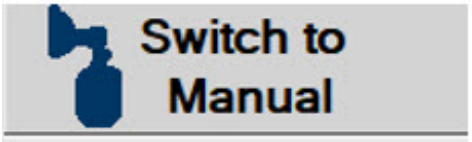
	Stop Calibration	Press this button to stop the calibration in the middle of a calibration process. The previous calibration will remain to be used.
	Calibration History	Press this button to display the history of calibration.
	Events	Press this tab to access the events menu.
	Clear Events	Press this button to clear the events listed on the events screen.
	Settings	Press this tab to access the settings screen.
		Press this button to begin the process of shutting down the Console.
		Press this button to switch display to day mode.
	Manual Mode Flow Rate (LPM): 10	This drop-down menu allows operator to preset the dilution flow rate for Manual Mode. If no rate is selected, Console will default to 10 LPM.
	Change Date Time	Press this button to enter the screen to adjust the date and time. This button is only present when logged as an Administrator
	Use Time Offset	Press this button to adjust the date and time. This button is only present when logged as an Administrator
	Perform Leak Test	Press this button to perform a Water Trap/ Sample Line Leak Test.
	Admin / Service Area	Used by service personnel only. Password controlled. **NOTE** Call Technical Support at **877-337-4118**for additional support.
	Display Dosing Usage	Press this button to display a window to enter date ranges to retrieve dosing usage over a period of time and number of Cassette activations.

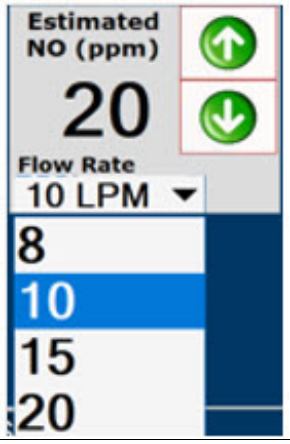
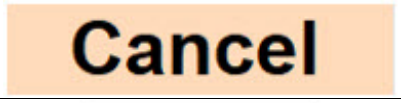
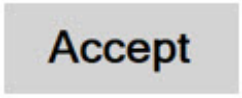
		Day Mode Main Menu: Press this tab to access the sub-level tabs (Main, Alarms, Calibration, Events, and Settings).
		Press this button to switch display from day mode to regular mode.

2.9 Display Screen Operational Buttons

The following buttons on the display screens allow the Operator to operate and adjust the GENOSYL DS prior to and during the delivery of nitric oxide.

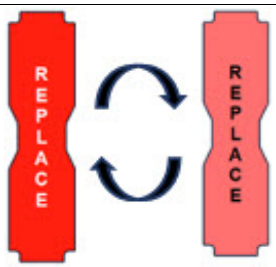
Note: the following are shown in "regular mode" but are also available in "day" mode.

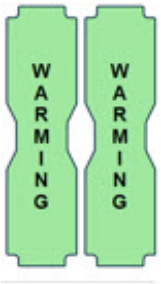
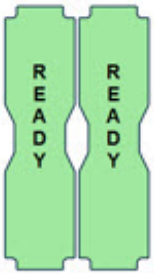
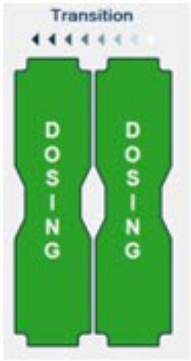
BUTTON	DESCRIPTION
	Press this button to set the targeted NO (ppm) dose when in Primary Mode.
	Press this button to pre-silence alarms. Pushing this button will pre-silence specific alarms for 120 seconds. When active, a red "X" will appear through the alarm icon with a countdown of how much longer alarms will be pre-silenced for. When tapping the icon with the red "X", the user will cancel the pre-silence.
	Press this button to cancel the Water Trap / Sample Line Leak Test.
	Press this button to switch a Console to Primary Mode from Manual Mode. When in Primary Mode, the dosage can be set to a user selected (prescribed) level.
	Press this button to switch from Primary Mode to Manual Mode. See Section 5.4for information about dosing in Manual Mode.
	Electronic keypad used to set and adjust the prescribed targeted Nitric Oxide dose to be delivered to the patient. Includes buttons to confirm (OK), cancel, or clear the entry.

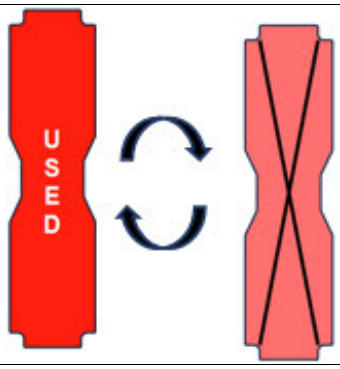
	The Total Flow Range is selected by the user if the Adaptive Sensor is not connected to the Console. These buttons will only appear if the Console does not detect an Adaptive Sensor when setting or adjusting dose. Total Flow range is the sum of the ventilator (or ancillary equipment) Bias Flow and the minute ventilation of the patient.
	Displayed when in Manual Mode, press the green up or down arrows to adjust the dose to the patient, from the default dose. Pressing the down arrow will decrease the dose in increments of 1 ppm for 24 ppm and below. Pressing the up arrow will increase the dose in increments of 2 ppm above 24 ppm. Press the green LPM (liters per minute) button to activate a drop-down menu and set a different dilution flow rate.
	Press this button to confirm the action specified on the screen.
	Press this button to cancel the action specified on the screen.
	Press this button to acknowledge the information message displayed on the screen.
	Press this button to move to the next step.
	Press this button to cancel the current step.

2.10 Display Screen – Cassette Status Indicators

The following describes the Cassette Status Indicators that will be shown on the display screen prior to, during, and post-delivery of nitric oxide. The Cassette Status Indicators consist of two Cassette icons, which correspond to the left and right Cassette receptacles.

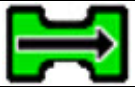
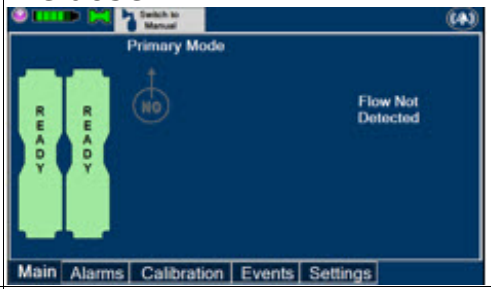
CASSETTE DISPLAY	DESCRIPTION
	This Cassette Status Indicator will be displayed when a Cassette is not loaded into the Console. The Cassette Status Indicator will display "REPLACE" and will alternate between a dark red and light red. The user is prompted to "Replace"

	This Cassette Status Indicator is displayed during the warmup phase when a new Cassette is inserted. This Indicator will display "WARMING" alternating with "READY". Dose may be initiated while the Cassette is warming.
	This Cassette Status Indicator is displayed once the Cassette has achieved a fully preheated status.
 	This Cassette Status Indicator is displayed during dosing. If a secondary Cassette has been inserted, the Cassette Status Indicator will display "Dosing" for the dosing Cassette and "Ready" for the secondary Cassette. If a secondary Cassette has not been inserted, the Cassette Status Indicator will display the percentage of Nitric Oxide remaining in the dosing Cassette and the secondary Cassette Status Indicator will be red and display "Replace".
	This Cassette Status Indicator will be displayed when the Console is transitioning from the dosing Cassette to the secondary Cassette. The direction of the arrow indicates the Cassette that is being transitioned to.
	This Cassette Status Indicator will be displayed when less than one hour of Cassette life remains and no secondary Cassette is inserted. The indicator will display the percentage of life remaining in the dosing Cassette and the estimated time before depletion. The cassette status indicator for the dosing Cassette will appear yellow and display "Dosing" and the other Cassette Status Indicator will appear red and display "Replace"

	This Cassette Status Indicator is displayed when a Cassette is depleted and no secondary Cassette is inserted in the Console. *This status will only display if another Cassette is not present in the Console.* The Cassette Status Indicator for the dosing Cassette will appear red and display "Dosing 0%" and "0m". The empty Cassette Status Indicator will appear red and display "Replace". Both indicators will alternate between a dark and light red color.
	This Cassette Status Indicator will be displayed when a Cassette that has previously been used is inserted in a Console. The Cassette display will alternate between "USED" and an "X" through the Cassette icon. The Console will automatically eject a previously used Cassette.

2.11 Display Screen - Adaptive Sensor Status

The following describes the Adaptive Sensor status that will be shown on the display screen. The Adaptive Sensor Icon is located on the top left of the Console display screen.

ADAPTIVE SENSOR DISPLAY	DESCRIPTION
	The Console has detected flow through the Adaptive Sensor.
	The Console has detected an Adaptive Sensor without flow. "Flow Not Detected" will be displayed under the dose set button when ventilator flow is not detected. To initiate delivery, the Console requires flow detection. The Set button will not appear until flow is detected through the Adaptive Sensor. The screen will appear as pictured below. Once flow is detected, the set button will appear and allow the user to set the dose. 

	The Console does not detect an Adaptive Sensor is connected
	An Adaptive Sensor is detected but the Adaptive Sensor is either malfunctioning or not properly connected to the Adaptive Sensor Cable.

2.12 Cassette Insertion into Console

When inserting a Cassette into a Console, it is important to push the Cassette fully into the receptacle and confirm the Cassette has been registered on the screen.

PHOTO	DESCRIPTION
	Insert the Cassette into the receptacle. Push in until you hear the Cassette click into the mechanism.
	The on-screen Cassette Status Indicator will switch to say "READY" and then prompt the user to begin a Water Trap/ Sample Line Leak Test.

2.13 Water Trap / Sample Line Leak Test

A Water Trap / Sample Line Leak Test is initiated when a Cassette has been inserted into the Console and fully seated, and if the measured NO is less than 1.0 ppm. Its purpose is to test the integrity of the Water Trap seal, the proper seating of the Water Trap, and the Sample Line connection to each Console, prior to operation. This is important to ensure an accurate measurement of NO within the ventilator circuit.

After the test has been initiated, the screen will prompt the Operator to close the Stopcock Valve and the Operator will have **60 seconds within which to do this**. A numerical timer and a horizontal progress bar provide a visual representation of the time elapsed (red) and time remaining (gray). Once the Stopcock Valve has been closed and if the test has been successfully completed, the entire progress bar will turn green.

TEST IN PROCESS	TEST PASSED

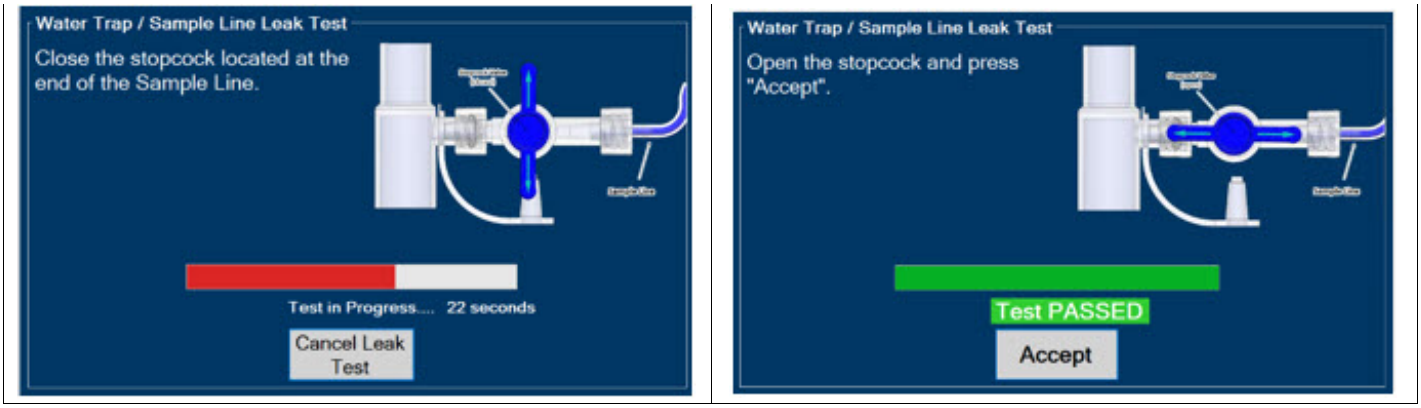


Figure 14: Water Trap/Sample Line Leak Test

If the test has failed, the progress bar will remain red throughout the full 60 seconds. The Operator will be notified and prompted to troubleshoot the potential cause

Prior to completion of the leak test and if a condition exists in which immediate NO delivery is required, the Operator may cancel the leak test. The GENOSYL DS will allow a dose of 20 ppm to be set in Primary Mode. If a different dose is required, a Water Trap/Sample Line Leak test must be completed.

The Water Trap/ Sample Line Leak Test may also be initiated manually via the Settings Tab and pressing the "Perform Leak Test" button. This may be useful to test the integrity of the Water Trap and Sample Line independent of the need to initiate the delivery of Nitric Oxide (see Settings in Section 2.8).

SECTION 3
SYSTEM SET-UP AND CONNECTIONS

3. SYSTEM SET-UP AND CONNECTIONS

3.1 GENOSYL DS Set-Up and Mechanical Ventilator Circuit Schematic

NOTE
Naming conventions: The GENOSYL DS accessories and components consist of the GENOSYL Injection Assembly with Adaptive Sensor, (Section 3.4), or the GENOSYL DS Mixer Assembly with Adaptive Sensor (Section 3.5), and the GENOSYL DS Gas Lines (Section 3.6). Refer to Section 10.2 Table 10 for when use of the Mixer Assembly with Adaptive Sensor is recommended. Connections and disposable circuits to breathing Systems may vary and are unique to individual manufacturers. Example circuit diagrams are provided for reference.

The schematic in Figure 15 shows an example ventilator circuit set-up and connection to

the GENOSYL DS, and a manual ventilation bagging system.

All required GENOSYL DS Parts / Components are listed in the front of this manual and should be removed from their packaging prior to set-up.

3.2 Connections to Various Breathing Systems

WARNING
• ALWAYS use the GENOSYL DS in accordance with the indications, usage, contraindications, warnings, and precautions described in the GENOSYL prescribing information and labeling. Refer to latest approved prescribing information and labeling prior to use. • The approved patient population for the GENOSYL DS as specified in the drug labeling for GENOSYL (nitric oxide) for inhalation, is limited to neonates. The GENOSYL DS is not intended to be used in other patient populations. • ONLY use the GENOSYL DS, its parts, and accessories as instructed. Using non-specified components may result in product malfunction, injury or death. • ALWAYS follow pre-use setup instructions for the routing and connections of tubing to avoid patient strangulation. • MAKE SURE the System has all tubing connected as described in the instructions. Not connecting all tubing may result in inaccurate dosage and harm to the patient. • DO NOT use accessories or cables other than those specified or provided by the manufacturer of this equipment, as this may result in increased electromagnetic emissions or decreased electromagnetic immunity of this equipment and result in improper operation.

CAUTION
Prolonged use in dry environments without humidification will damage the gas sensors. Supplemental humidification providing greater than 20% relative humidity (RH) in the patient circuit is recommended.

NOTE
All circuit components, including GENOSYL DS circuit components, should be changed out and disposed of according to hospital protocol.

3.2.1 Conventional Ventilators

Compatibility testing has demonstrated performance meeting requirements for the GENOSYL DS operating range of 0 to 80 ppm with the following conventional ventilators at the operating ranges shown in Table 1 .For further information on the use of the GENOSYL DS with validated MR conditional ventilators in the MR environment, refer to Section 7.

- Bio-Med Devices CrossVent 2+/2i+
- Bio-Med Devices MVP-10
- Dräger V500
- Dräger VN500
- GE Healthcare R860
- Hamilton C1/T1

- Hamilton C2/C3
- Hamilton G5
- Hamilton MR1
- Maquet Servo-U/N/I
- Maquet Servo-I MR
- Puritan Bennett 840
- Puritan Bennett 980
- Vyaire AVEA

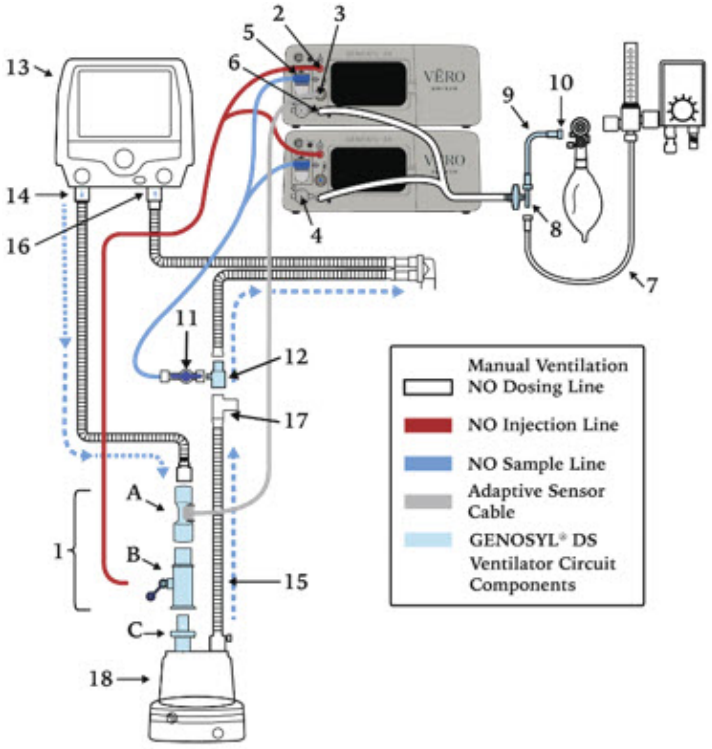
WARNING
ONLY use the GENOSYL DS with Bio-Med Crossvent 2+/2i+ with Constant Flow ON. Not doing so may lead to elevated NO_2 levels or dose variability.

NOTE
• Use with Compliance Compensation OFF is recommended in the presence of a deliberate leak, per the Servo-I User Manual. With Compliance Compensation ON, the sample flow from the GENOSYL DS may cause a leak detection alarm to trigger for the lowest potential ventilator flows. • For use with Hamilton C2/C3 at pediatric/adult ventilator settings, it is recommended that the 2.5 to 10 LPM Total Flow setting be used for Nitric Oxide dosing, when not using an Adaptive Sensor.

Table 1: Conventional Ventilator Compatibility Test Ranges

Setting	Range	Unit
Inspiratory Flow Rate	2-120	LPM
Respiratory Rate	6-60	BPM
Peak Inspiratory Pressure	0-70	cmH_2O
Positive End Expiratory Pressure	0-20	cmH_2O

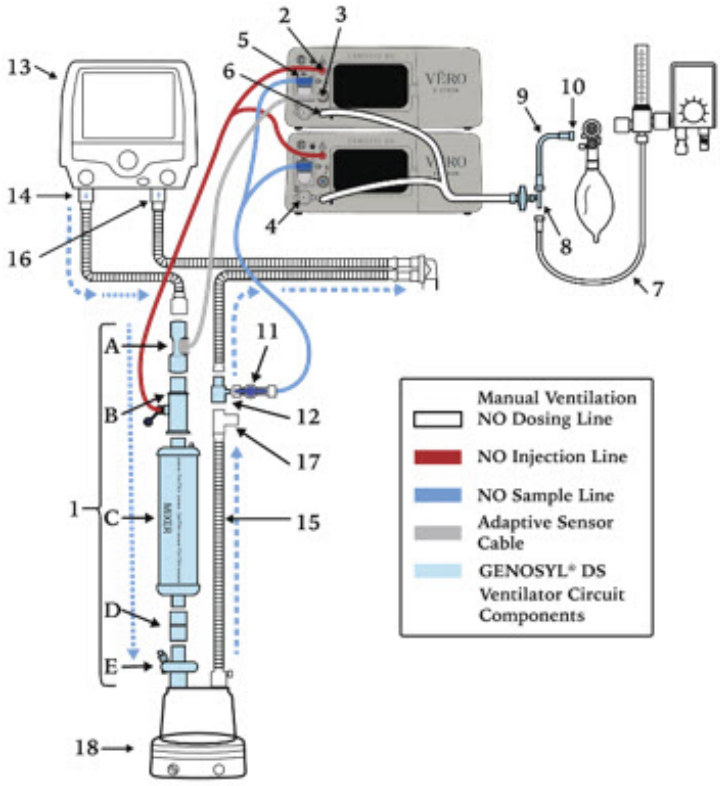
The ventilator circuit diagram for use <u>without</u>the Inline Mixer Accessory, required in certain scenarios, is shown in Figure 15. See Section 10.2, Table 10for applicable use scenarios.



1. Injection Assembly with Adaptive Sensor*
    A. Adaptive Sensor
    B. NO Gas Injection Adapter
    C. Inline Breating Circuit Filter
2. GENOSYL (nitric oxide) Port
3. Adaptive Sensor Port
4. Calibration Port
5. Water Trap
6. Manual Ventilation NO Dosing Port
7. Oxygen Tubing
8. Oxygen Tubing Connection with Filter
9. Manual Ventilation Bag NO Adapter
10. Manual Ventilation Bag Connector
11. Stopcock
12. Gas Sample Tee
13. Ventilator
14. Ventilator Inspiratory Outlet
15. Inspiratory Limb
16. Ventilator Expiratory Inlet
17. Temperature Port Probe
18. Humidifier

*See Section 3.4.1 for detailed assembly instructions for the Injection Assembly with Adaptive Sensor

The ventilator circuit diagram for use <u>with</u>the Inline Mixer Accessory, required in certain scenarios, is shown in Figure 1 <u>6</u>. See Section 10.2, Table 10for applicable use scenarios.



1. Mixer Assembly with Adaptive Sensor*
    A. Adaptive Sensor
    B. NO Gas Injection Adapter
    C. Mixer
    D. Adapter (22F X 22F)
    E. Inline Breathing Circuit Filter
2. GENOSYL (nitric oxide) Port
3. Adaptive Sensor Port
4. Calibration Port
5. Water Trap
6. Manual Ventilation NO Dosing Port
7. Oxygen Tubing
8. Oxygen Tubing Connection with Filter
9. Manual Ventilation Bag NO Adapter
10. Manual Ventilation Bag Connector
11. Stopcock
12. Gas Sample Tee
13. Ventilator
14. Ventilator Inspiratory Outlet
15. Inspiratory Limb
16. Ventilator Expiratory Inlet
17. Temperature Port Probe
18. Humidifier

*See section 3.4.2 for detailed assembly instructions for the Mixer Assembly with Adaptive Sensor

3.2.2 Non-Invasive Gas Delivery Systems

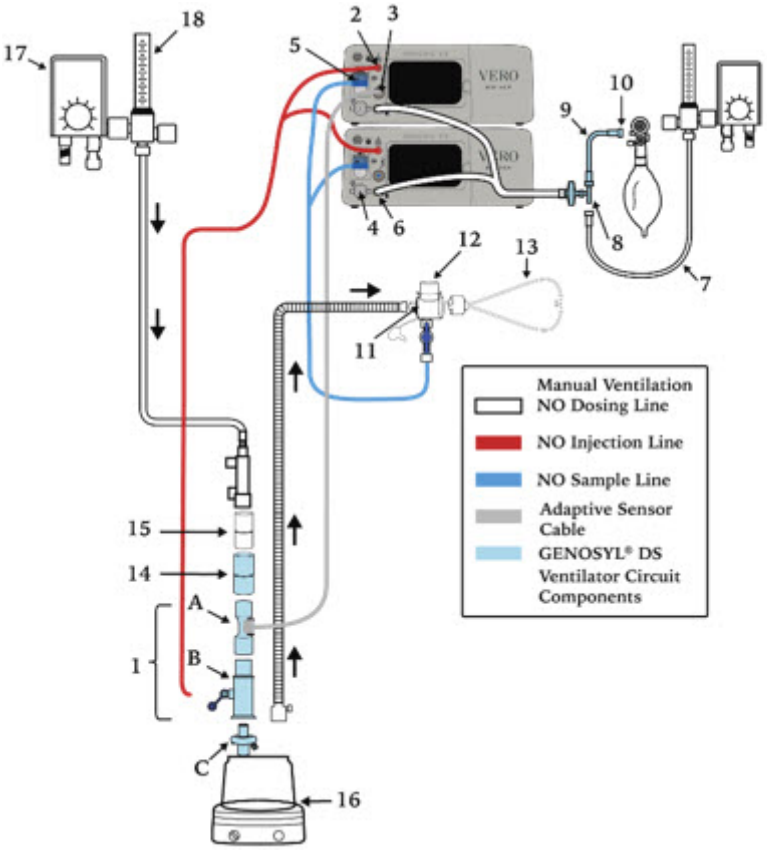
Compatibility testing has demonstrated performance meeting requirements for the GENOSYL DS operating range of 0 to 80 ppm with the following non-invasive gas delivery systems at operating ranges shown in Table 2.

- Fisher and Paykel Optiflow Jr Breathing Circuit
- Fisher and Paykel Optiflow Breathing Circuit
- Infant Bubble Continuous Positive Airway Pressure (CPAP)

Table 2: Non-Invasive Gas Delivery System Compatibility Test Ranges

Setting	Range	Unit
Optiflow Jr Flow Rate	0.75-36	LPM
Optiflow Flow Rate	3-60	LPM
Bubble CPAP Continuous Flow Rate	4-15	LPM
CPAP Pressure	3-10	cmH $_2$O

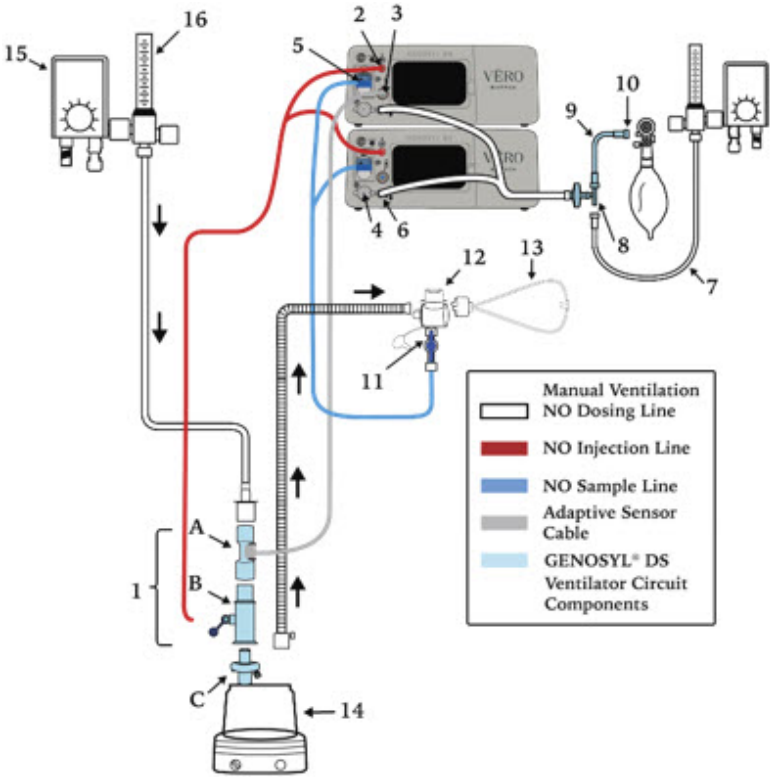
The Fisher and Paykel Optiflow Jr Breathing Circuit for use with the GENOSYL DS is shown in Figure 17.



1. Injection Assembly with Adaptive Sensor*
   - A. Adaptive Sensor
   - B. NO Gas Injection Adapter
   - C. Inline Breathing Circuit Filter
2. GENOSYL® (nitric oxide) Port
3. Adaptive Sensor Port
4. Calibration Port
5. Water Trap
6. Manual Ventilation NO Dosing Port
7. Oxygen Tubing
8. Oxygen Tubing Connection with Filter
9. Manual Ventilation Bag NO Adapter
10. Manual Ventilation Bag Connector
11. Stopcock
12. Optiflow Jr Adapter (REF OPT016)
13. Optiflow Jr Cannula
14. Adapter (22F X 22F)
15. Adapter (22M X 22M)
16. Humidifier
17. Air /Oxygen Blender
18. Flowmeter

*See Section 3.4.1 for detailed assembly instructions for the Injection Assembly with Adaptive Sensor

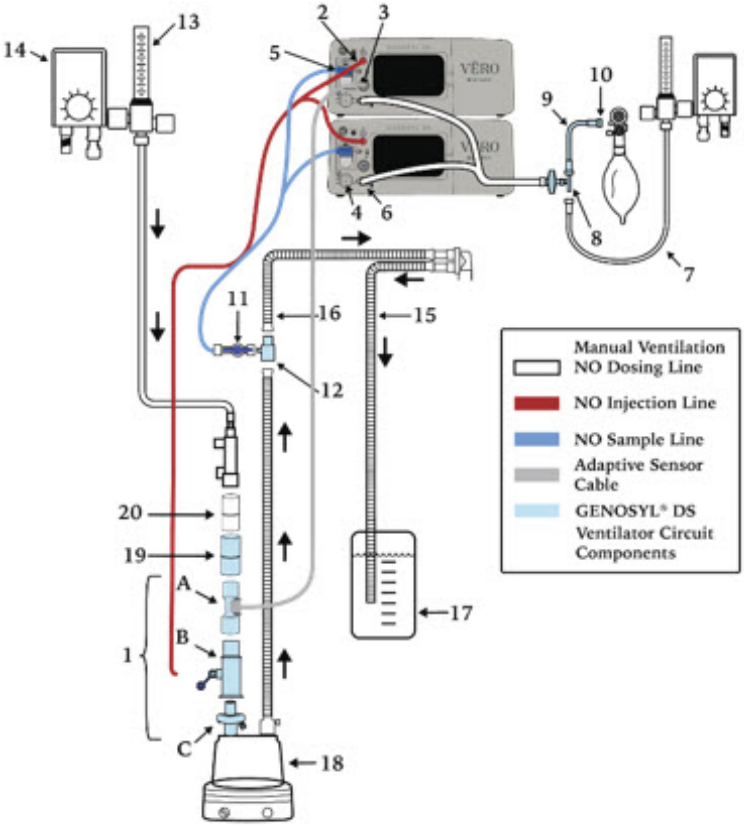
The Fisher and Paykel Optiflow Breathing Circuit for use with the GENOSYL DS is shown in Figure 18.



1. Injection Assembly with Adaptive Sensor*
   A. Adaptive Sensor
   B. NO Gas Injection Adapter
   C. Inline Breathing Circuit Filter
2. GENOSYL® (nitric oxide) Port
3. Adaptive Sensor Port
4. Calibration Port
5. Water Trap
6. Manual Ventilation NO Dosing Port
7. Oxygen Tubing
8. Oxygen Tubing Connection with Filter
9. Manual Ventilation Bag NO Adapter
10. Manual Ventilation Bag Connector
11. Stopcock
12. Optiflow Jr Adapter (REF OPT016)
13. Optiflow Cannula
14. Humidifier
15. Air/Oxygen Blender
16. Flowmeter

*See Section 3.4.1 for detailed assembly instructions for the Injection Assembly with Adaptive Sensor

The infant bubble CPAP diagram for use with the GENOSYL DS is shown in Figure 1 9.



1. Injection Assembly with Adaptive Sensor*
   A. Adaptive Sensor
   B. NO Gas Injection Adapter
   C. Inline Breathing Circuit Filter
2. GENOSYL (nitric oxide) Port
3. Adaptive Sensor Port
4. Calibration Port
5. Water Trap
6. Manual Ventilation NO Dosing Port
7. Oxygen Tubing
8. Oxygen Tubing Connection with Filter
9. Manual Ventilation Bag NO Adapter
10. Manual Ventilation Bag Connector
11. Stopcock
12. Gas Sample Tee
13. Flowmeter
14. Air/Oxygen Blender
15. Expiratory Limb
16. Inspiratory Limb
17. Bubble Jar
18. Humidifier
19. Adapter (22F X 22F)
20. Adapter (22M X 22M)

*See Section 3.4.1 for detailed assembly instructions for the Injection Assembly with Adaptive Sensor

3.3 GENOSYL DS Ventilator Circuit Assembly Pre-Check

Follow the steps listed below for the initial System pre-check prior to completing the ventilator circuit assembly.

ILLUSTRATION	ACTION	Warnings, Cautions and Notes
• **Cassettes**– 2 ea. • **Adaptive Sensor**– 1 ea. • **Adaptive Sensor Cable**– 1 ea. • **Gas Injection Adapter**– 1 ea. • **Inline Breathing Circuit Filter**1ea. • **Mixer Assembly** ◦ **Mixer**– 1 ea. ◦ **Adapter**(22mm ID × 22mm ID) – 1ea. ◦ **Inline Breathing Circuit Filter**– 1 ea. • **Gas Lines**– 1 ea. • **Gas Sample Tee**– 1 ea. • **Manual Ventilation Bag NO Adapter**– 1 ea.	1. **Remove**all items of the GENOSYL DS Parts / Components from packaging. 2. **Check**the expiration date for **each Cassette and the Inline Breathing Circuit Filter**(if Mixer Assembly is used) to ensure use is within the expiration date.	**WARNING** DO NOT use a Cassette that is beyond its expiration date. Using an expired Cassette may affect the Cassette's ability to provide the correct NO dosage to the patient, which may cause injury or death. **NOTE** A Mixer Assembly is not required for all use cases. Refer to Section 10.2, Table 10)
		WARNING ALWAYS empty Water Trap before each use, when prompted by the

	1. Visually **inspect** the Water Traps on **both Consoles** to ensure they are installed and empty.	prompted by the System, and when the trap is more than half full. Allowing the Water Trap to completely fill will occlude the Sample Line which will interrupt patient gas NO, NO_2, and O_2 concentration monitoring. Failure to monitor the patient gas NO, NO_2, and O_2 concentrations may result in patient injury. ALWAYS conduct Water Trap/ Sample Line Leak Test every time you empty and replace the Water Trap, as failure to do so may lead to an incorrect NO reading, which can result in injury or death. **NOTE** To empty the Water Trap, see Section 9.4.1

3.4 Assembling GENOSYL DS Injection Assembly with Adaptive Sensor and GENOSYL DS Mixer Assembly with Adaptive Sensor

The Injection Assembly with Adaptive Sensor or the Mixer Assembly with Adaptive Sensor is the point of Nitric Oxide injection into the patient respiratory circuit. Only one type of assembly is required for each patient circuit. For certain scenarios, the Mixer Assembly with Adaptive Sensor is recommended to mix the NO gas with the gas supplied by the ventilator through a filter containing silica gel to provide intra-breath NO delivery. Refer to Section 10.2, Table 10 for scenarios when a Mixer is recommended for use.

NOTE
When using a Mixer, an Inline Breathing Circuit Filter must be used. If a Mixer is not used, an Inline Breathing Circuit Filter as presented in Figure 20 may be used, or an Injection Line Filter connected to the port on the Gas Injection Adapter may be used.

3.4.1 GENOSYL DS Injection Assembly with Adaptive Sensor

Follow the instructions outlined below to assemble the GENOSYL DS Injection Assembly as shown in Figure 20.

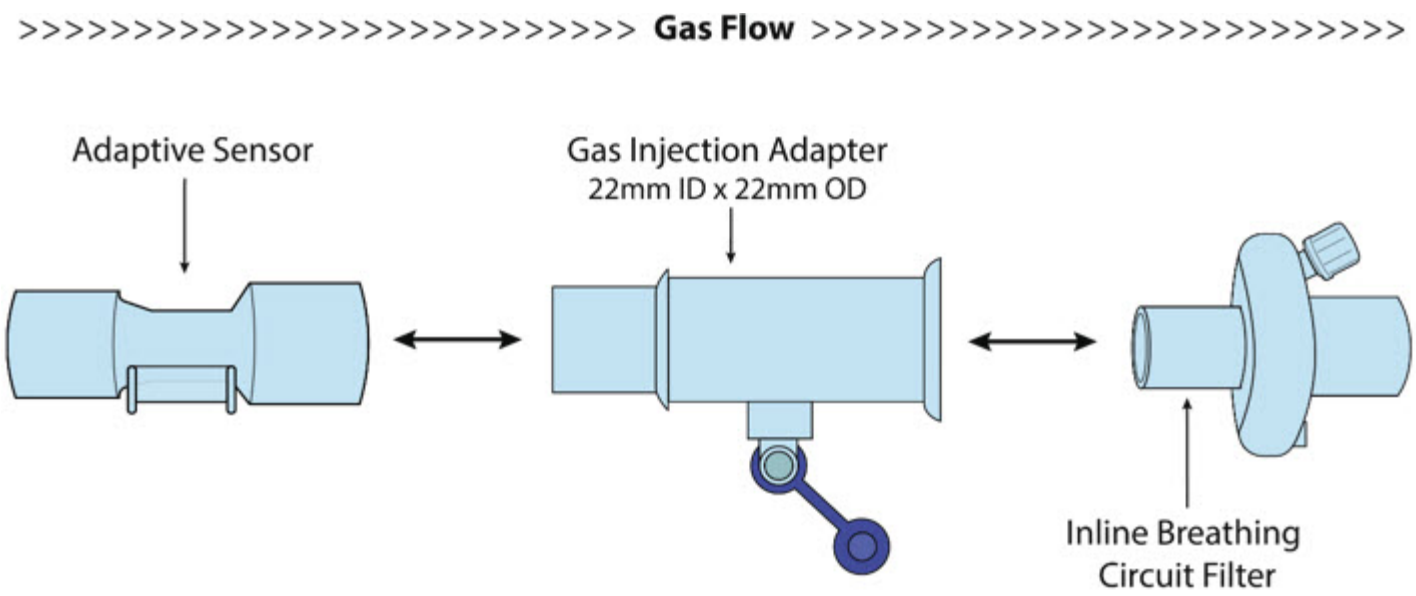
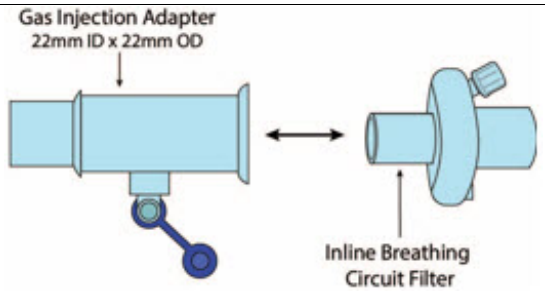
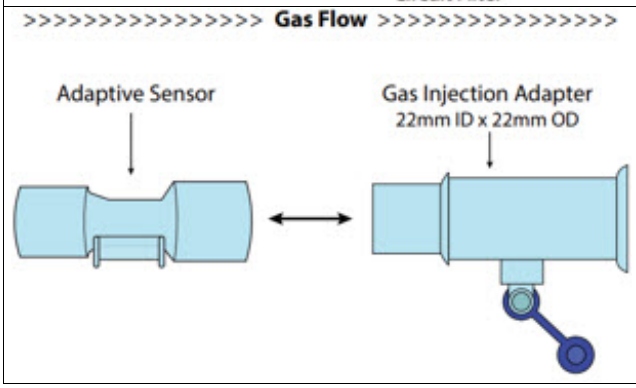


ILLUSTRATION	ACTION
	1. **Connect**the Inline Breathing Circuit Filter to the Gas Injection Adapter (22 mm ID × 22 mm OD).
	1. **Connect**the Adaptive Sensor to the inlet end of Gas Injection Adapter (22mm ID × 22 MM OD).

3.4.2 GENOSYL DS Mixer Assembly with Adaptive Sensor

If required, follow the instructions outlined below to assemble the GENOSYL DS Mixer Assembly with Adaptive Sensor as shown in Figure 2 1.

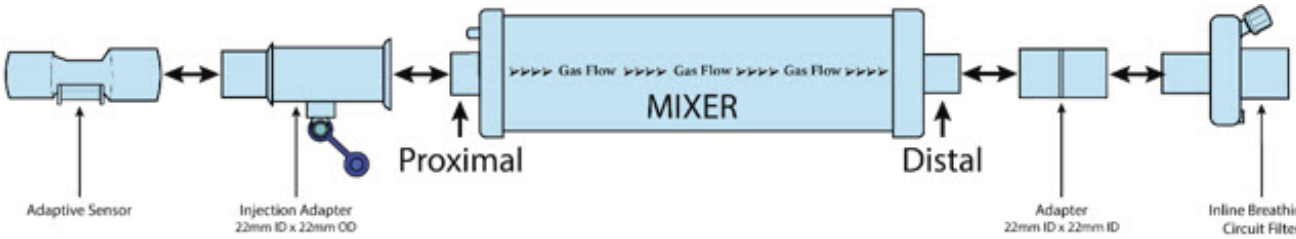
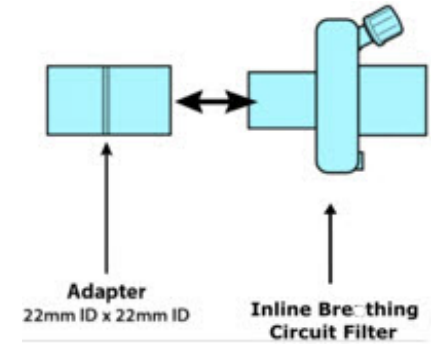
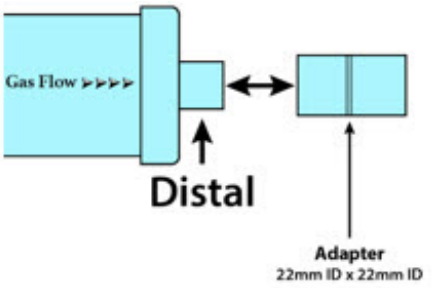
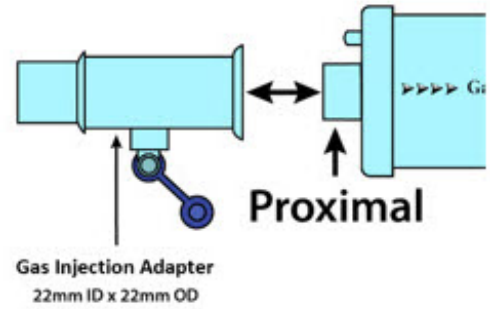
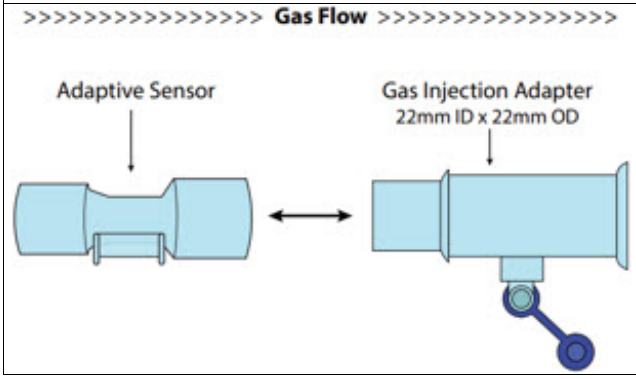
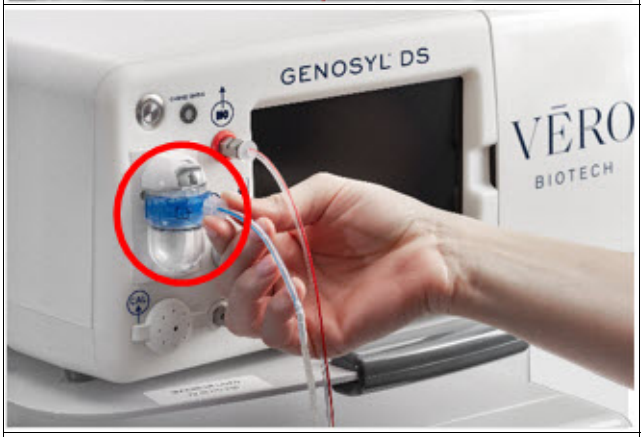


ILLUSTRATION	ACTION
	1. **Connect** the Inline Breathing Circuit Filter to the Gas Injection Adapter 22mm ID × 22 mm OD.
	1. **Connect** the Adapter (22mm ID × 22 mm ID) to the distal end of the Mixer.
	1. **Connect** the Gas Injection Adapter to the proximal end of the Mixer.
	1. **Connect** the Adaptive Sensor to the proximal end of the Gas Injection Adaptor

3.5 GENOSYL DS Console Connections

3.5.1 GENOSYL DS Gas Line Connections

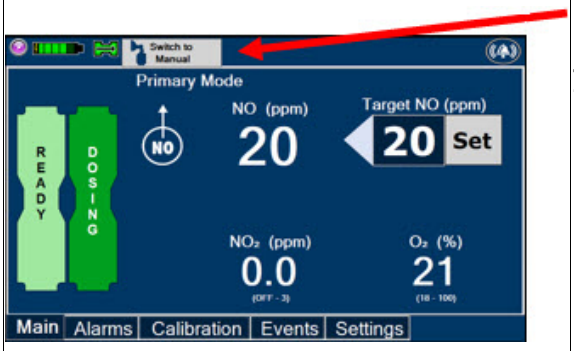
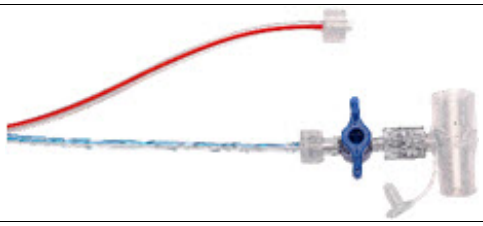
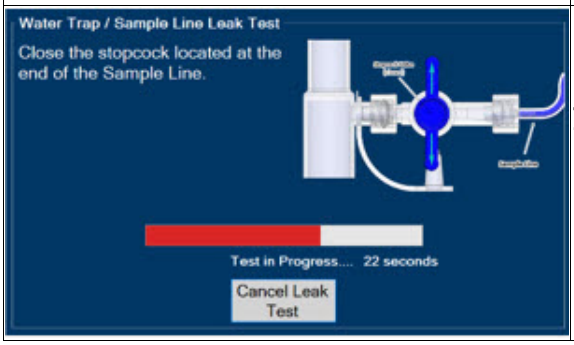
Follow the steps listed below to connect the GENOSYL DS to both Consoles.

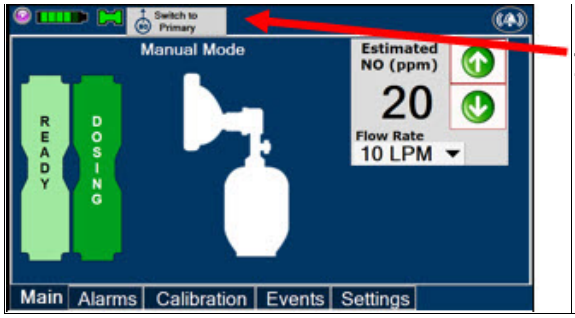
ILLUSTRATION	ACTION	Warnings, Cautions and Notes
	1. **Push**and **twist**clockwise the short Y-end of the NO Injection Line (red) to the **"NO" port (red)**on the front panel of the top Console.	
	1. **Push**and **twist**the short Y-end of the Sample Line (blue) to the **Gas Sample Port (blue)**on the front of the Water Trap, attached to the top Console.	**NOTE** Ensure the Sample Lines are connected to the **Water Traps on both Consoles.**
	1. Push and twist clockwise the end of the Manual Ventilation Line (clear) to the **Manual Ventilation Port (clear)**on the front panel of the top Console 2. **Repeat**steps 1, 2, and 3 on the bottom Console.	

3.5.2 GENOSYL DS Sample Line Extension Connection

For use in the MR Environment, where a longer sample line is required follow the steps listed below to connect a Sample Line Extension. It is recommended to install the Sample Line Extension prior to initiation of dose.

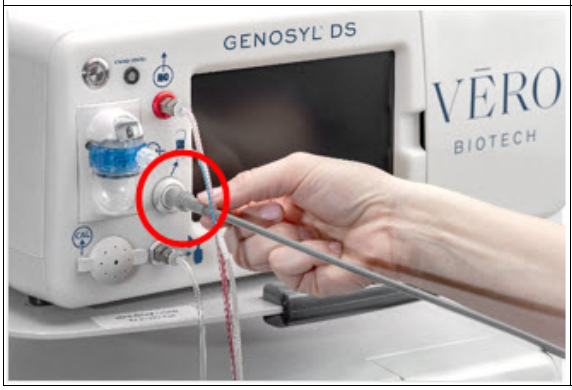
ILLUSTRATION	ACTION	Warnings, Cautions and

		Notes
	1. If actively dosing, **switch** to Manual prior to completing the following steps (see Section 5.4for details on Manual Mode).	**WARNING** Failure to switch to Manual Mode prior to installing a Sample Line Extension when the System is actively dosing may result in a spike in the NO dose delivered to the patient.
	1. **Turn** the blue Stopcock Valve, attached at the Gas Sample Tee, to the closed position as shown.	
	1. **Push** and **twist** counterclockwise the Luer-Lock Collar of the Sample Line to remove from the blue Stopcock Valve at the Gas Sample Tee.	
	1. **Push** and **twist** clockwise the Luer-Lock Collar of the Sample Line onto the Sample Line Extension female connection. 2. **Push** and **twist** clockwise the Luer-Lock Collar of the Sample Line onto the blue Stopcock Valve at the Gas Sample Tee.	
	1. **Perform** Water Trap/Sample Line Leak Test, as detailed in Section 2.13.	

	1. If actively dosing, **<u>switch</u>**back to Primary mode (see Section 5.4.2for details on resuming Primary dosing).	

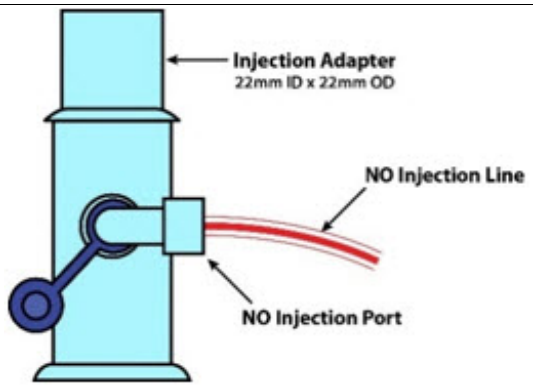
3.5.3 GENOSYL DS Adaptive Sensor Cable Connection

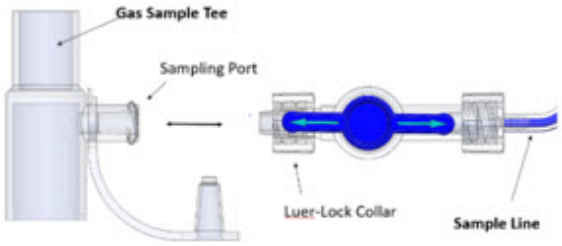
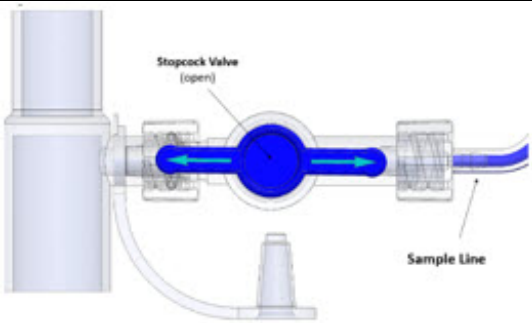
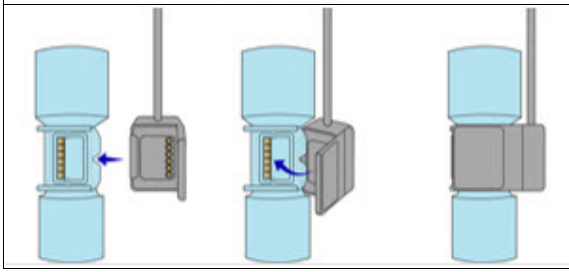
Follow the step below to connect the Adaptive Sensor Cable to the Dosing Console.

ILLUSTRATION	ACTION	Warnings, Cautions and Notes
	1. **<u>Connect</u>**the Adaptive Sensor Cable to the Adaptive Sensor Port on front of the Dosing Console.	**NOTE** The Adaptive Sensor should only be connected to the Dosing Console.

3.5.4 GENOSYL DS Respiratory Circuit Connections

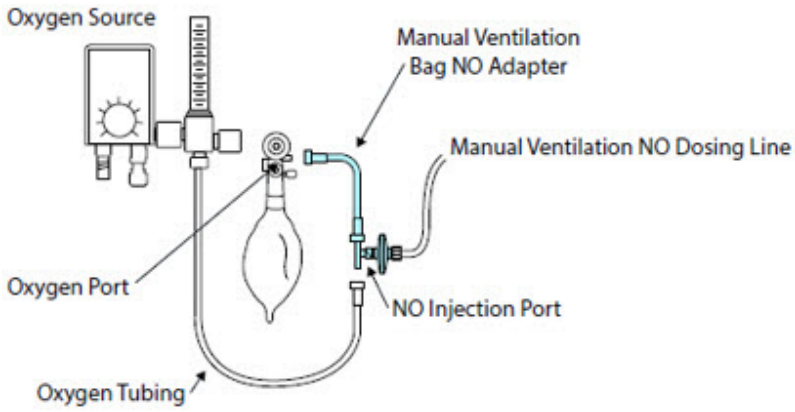
Follow the steps listed below to connect the Gas Lines to the Injection Assembly, Sample Tee, and Adaptive Sensor. If a Sample Tee already exists within the ventilator circuit, the Sample Line may be connected directly to the existing Sample Tee.

ILLUSTRATION	ACTION	Warnings, Cautions and Notes
	1. **<u>Push</u>**and **twist**clockwise the Luer-Lock Collar from the NO Injection Line onto the Injection Assembly.	**NOTE** After connecting, the valve assembly may have rotated such that the orientation may appear different from what is shown here and on the display screen.

	1. **Push**and **twist**clockwise the Luer-Lock Collar of the Sample Line onto the Sampling Port of the Gas Sample Tee.	**NOTE** Skip this step if a Gas Sample Tee is already connected and in-line with the ventilator circuit.
	1. **Ensure**the blue Stopcock Valve is in the open position as shown.	
	1. **Connect**the distal end of the Adaptive Sensor Cable to the Adaptive Sensor on the Injection Assembly	

3.6 Manual Ventilation (Bag) Connection

Follow the steps listed below to connect the Manual Ventilation Line to a manual bagging system.

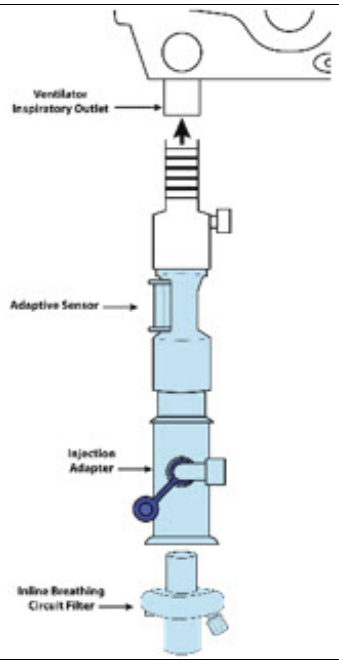
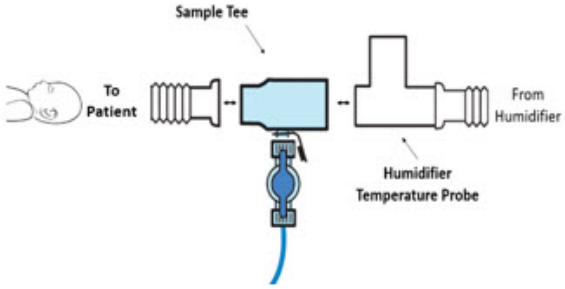
ILLUSTRATION	ACTION
	1. **Attach**the barbed end of the Manual Ventilation Bag NO Adapter into the oxygen tubing from the oxygen source. 2. **Attach**the other end of the NO Adapter to the oxygen port on the side of the Manual Ventilation Bag. 3. **Connect**the Manual Ventilation Line (clear) to the NO Injection Port of the Manual Ventilation Bag NO Adapter. 4. **Place**the Manual Ventilation Assembly in a clean accessible place if needed for future use.

3.7 Mechanical Ventilator Circuit Connections

Follow the steps outlined in this section to connect the GENOSYL DS Ventilator Circuit Assembly to the Mechanical Ventilator Circuit.

WARNING
• ALWAYS ensure the trigger sensitivity of the ventilator is checked after connecting the GENOSYL DS to the breathing circuit. The GENOSYL DS injects and samples gas from the patient respiratory circuit which may affect the triggering sensitivity of the ventilator. • ALWAYS ensure the patient disconnect and high–pressure alarms are used with the ventilator. Otherwise, the System is not working properly.

NOTE
All ventilator connections should be assembled and inspected prior to connecting to the mechanical ventilator circuit.

ILLUSTRATION	ACTION	Warnings, Cautions and Notes
	1. **Disconnect**the Inspiratory Tubing from the humidifier and attach it to the proximal end of the Injection Assembly to the Adaptive Sensor. 2. **Attach**the distal end of the Injection Assembly to the humidifier.	
	1. **Insert**the Sample Tee into the ventilator circuit at the proximal end of the temperature probe **closest to the patient.**	**NOTE** If a Gas Sample Tee is already connected and in-line with the ventilator circuit, connect the blue Sample Line directly to the existing Gas Sample Tee.

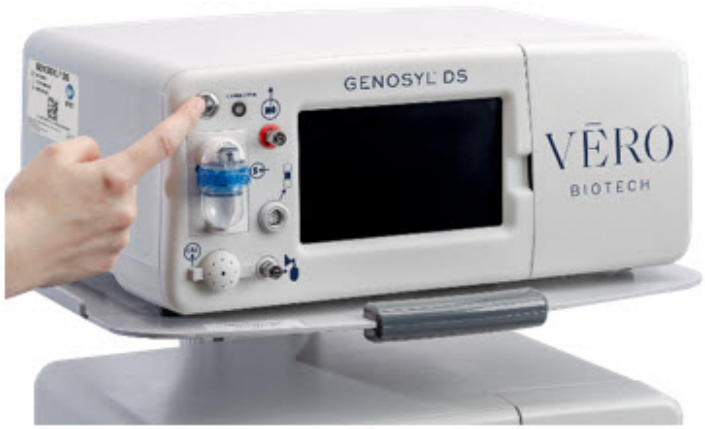
SECTION 4
SYSTEM START-UP

4. SYSTEM START UP

4.1 Console Start-Up

Follow the instructions in this section to turn on both the Dosing and Back-up Consoles.

ILLUSTRATION	ACTION	Warnings, Cautions and Notes
		CAUTION ONLY use the GENOSYL DS with the power cord supplied

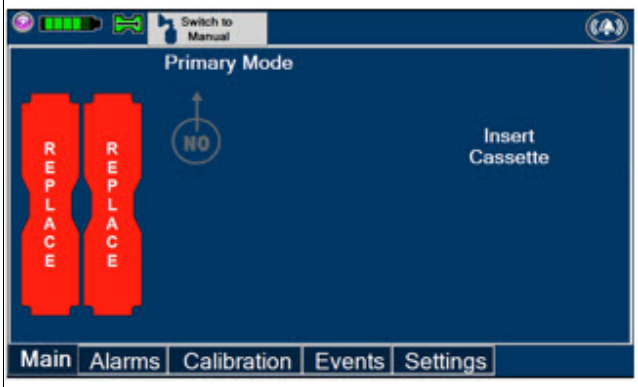
	1. **Push**the Circular Power Connectors into the back of the **top and bottom**Consoles. 2. **Connect**the main power cord to a grounded 120 V electrical outlet.	by the manufacturer. Use of a generic power cord may cause output voltage instability leading to a touch screen failure. ALWAYS ensure the power cord is firmly seated into the power supply and the wall outlet. A loose connection can result in damage to the device or faulty operation.
	1. **Press**the Black Rocker Power Switch, located on the back of **each**Console, to the right (ON position) to power on **both**Consoles.	
	1. **Press**the Silver Power Button, located at the top left corner on the front panel of **each**Console, to turn on the display screens on **both**Consoles. The display screen will illuminate, and the Consoles will beep, indicating the power is on.	**CAUTION** The System will conduct an internal self-test. If an alarm or failure message should occur, refer to Section 8 to resolve the issue. **NOTE** If the display screen does not turn on, see Troubleshooting, Section 8.7.

4.2 Cassette Insertion & Water Trap / Sample Line Leak Test

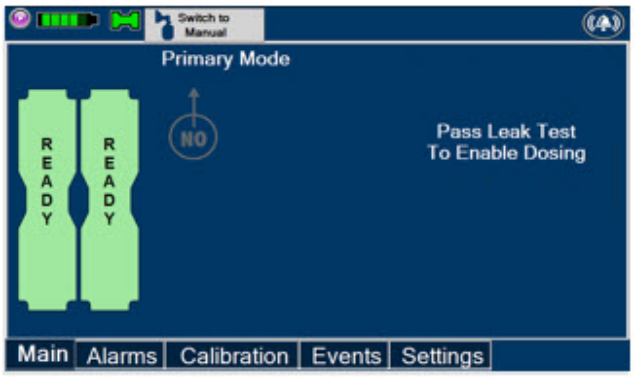
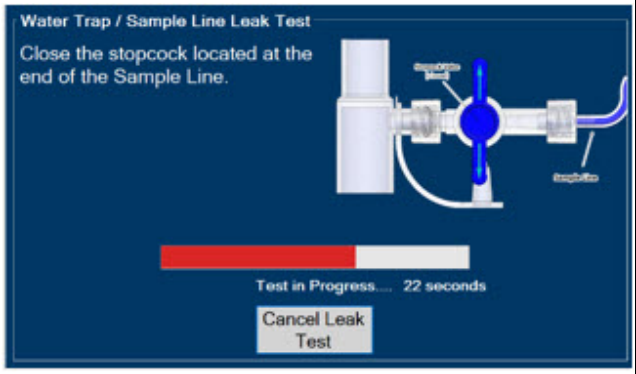
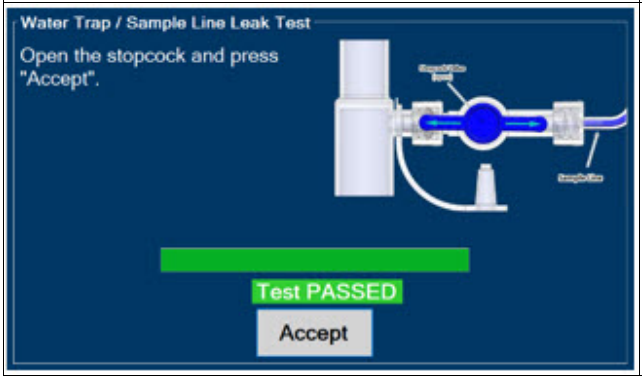
The following steps should be taken on both the top and bottom Consoles. Initiating Console Start-Up and inserting a Cassette for the bottom Console at this stage will prepare it to serve as a Back-up for the top Console.

Upon the insertion of a Cassette, a test will be initiated on each Console to check and ensure the integrity of the Water Traps and Sample Line (see Section 2.13). This helps ensure the accuracy of NO being delivered to the ventilator circuit.

The Water Trap/ Sample Line Leak Test is automatically initiated upon one or both of the following conditions: 1) Insertion and seating of the Cassette if the measured NO is less than 1.0 ppm and/or 2) Insertion and seating of the Water Trap.

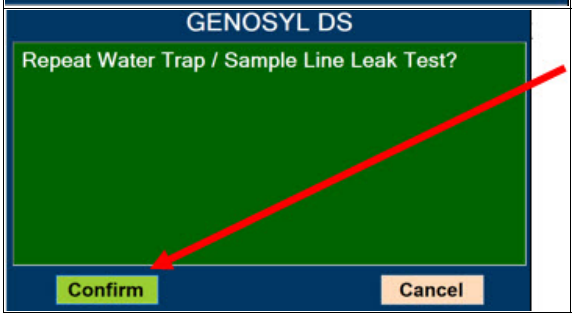
ILLUSTRATION	ACTION	Warnings, Cautions and Notes
	The following steps should be taken to insert the Cassettes into the Consoles.	**WARNING** ALWAYS follow Cassette inspection instructions prior to Cassette insertion. Not inspecting the Cassette prior to insertion may lead to using a faulty Cassette, resulting in injury. **NOTE** Upon turning on the Consoles, the Cassette Indicator will display "Replace"
		WARNING

	1. **Confirm**the Cassette State Window on **each**Cassette is blue.	**WARNING** DO NOT use the Cassette if the window is not blue. A Cassette State Window that is any color other than blue may affect the Cassette's ability to provide the correct NO dosage to the patient, which may cause injury or death. **NOTE** Cassette is inserted front first. The Cassette State Window is not visible when properly inserted. If the Cassette State Window is not blue, see Troubleshooting, Section 8.7.
	1. **Open**the Cassette Access Doors and insert two Cassettes into the Dosing Console and at least one Cassette into the Back-up Console. Push until it clicks.	**NOTE** Make sure Consoles are turned on before inserting the Cassette. The Water Trap / Sample Line Leak Test is **automatically initiated when the Cassette has been inserted**and the measured NO is less than 1.0 ppm. After the first Cassette **is fully inserted**, **the Operator will have 60 seconds to close the blue Stopcock Valve**to perform the test (Step 3below). Gas lines will need to be

		connected to the Console in order to pass the Water Trap/ Sample Line Leak Test.
		**NOTE** The Display Screen will temporarily indicate the Cassette has been detected, then automatically transition to the Water Trap / Sample Line Leak Test screen.
	1. **<u>Follow</u>**the onscreen instructions **on both Consoles.**	**NOTE** The screen will indicate the Water Trap / Sample Line Leak Test has started and the progress bar will be red until the stopcock valve has been closed, upon which it will then turn green if there is no leak detected. Pressing "Cancel Leak Test", will allow for dosing in Manual Mode. See Section 5.4for detail around dosing in Manual Mode.
	1. **<u>Follow</u>**the onscreen instructions **on both Consoles.**	**CAUTION** **Open the blue Stopcock Valve <u>prior</u>to pressing "Accept".** Failure to do so will result in a line occlusion alarm.

4.2.1 Water Trap / Sample Line Leak Test Troubleshooting

NOTE
If the Water Trap / Sample Line Leak Test fails, follow the onscreen instructions below to resolve the issue. Also see Troubleshooting, Section 8.7.

ILLUSTRATION	ACTION	Warnings, Cautions and Notes
	1. If this screen is displayed, **<u>follow</u>**the onscreen instructions **on both Consoles.**	
	1. **<u>Press</u>**Confirm on **both**Consoles to begin a new Water Trap / Sample Line Leak Test.	**NOTE** NO Injection is held at 20 ppm until the completion of a successful Water Trap / Sample Line Leak Test.

SECTION 5
NITRIC OXIDE ADMINISTRATION

5. NITRIC OXIDE ADMINISTRATION

5.1 Nitric Oxide Dose Set-Up and Administration

The following steps are a continuation of Section 4.2, in which the Cassette will now be activated for Nitric Oxide administration.

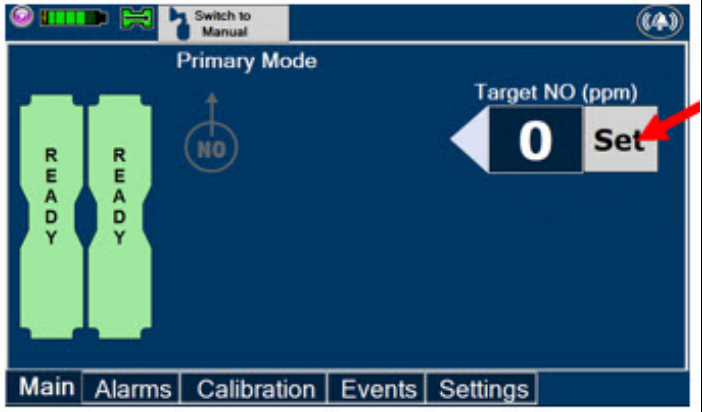
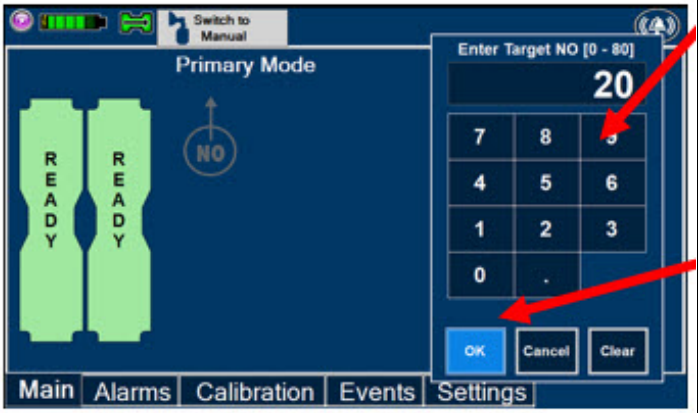
WARNING
• MAKE SURE the System stabilizes to the prescribed concentration (ppm) of NO prior to leaving the Console unattended. Failure to do so could result in under delivery of the target NO, leading to injury or harm. • ALWAYS constantly monitor the patient. System malfunctions can occur if device and

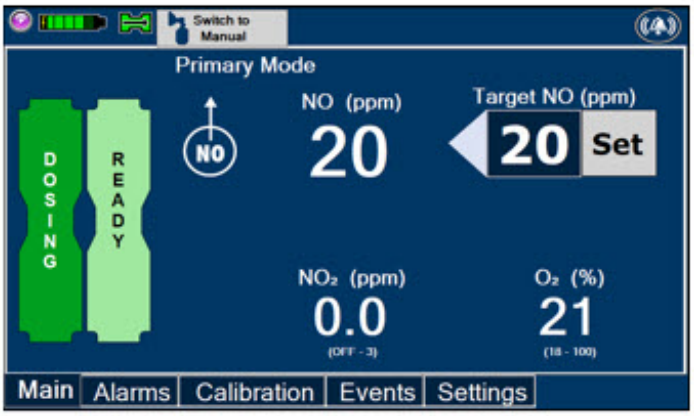
patient are not monitored and can result in injury or death. Careful monitoring is required by care personnel whenever the System is used on a patient. The use of an alarm and a monitoring system does not give an absolute assurance of warning for every malfunction that may occur. Certain alarms may require immediate response.

- If the gas flow of the patient's respiratory device/ventilator should be interrupted or discontinued, the NO dose should be maintained by switching to Manual Mode or the target NO dose should be set to zero.

5.1.1 Setting a Dose when using a Circuit***with***an Adaptive Sensor

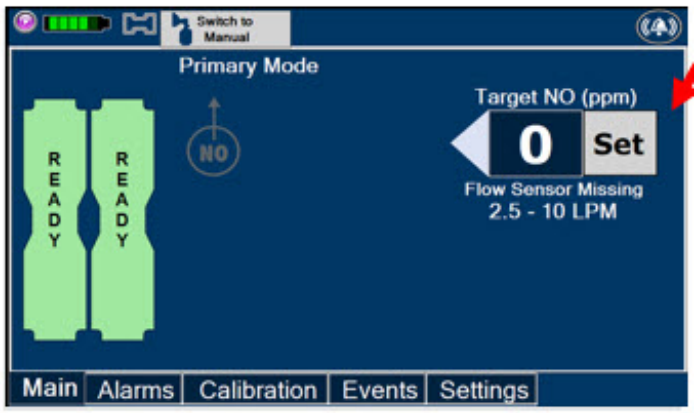
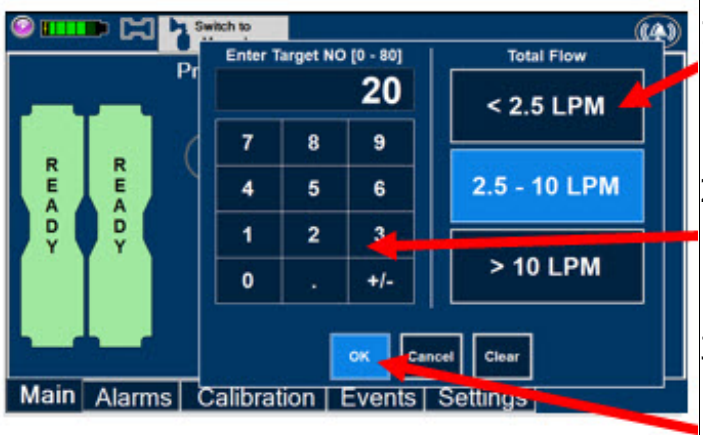
This section describes how to set a Nitric Oxide dose when an Adaptive Sensor is used in the patient circuit. Refer to Section 3.2 for recommended set up diagrams.

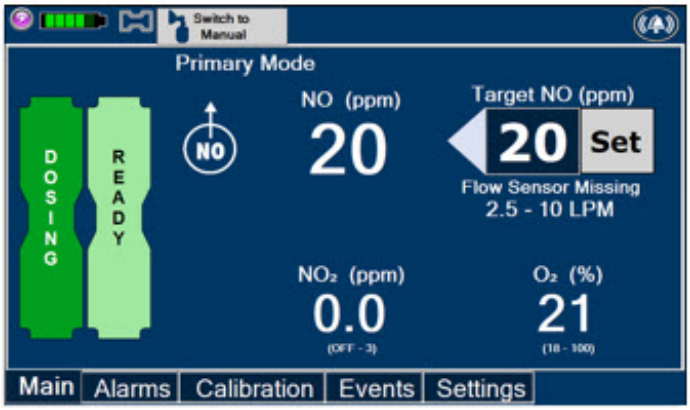
ILLUSTRATION	ACTION	Warnings, Cautions and Notes
	1. **Press**the gray "Set" button on the display screen.	**Note** The Adaptive Sensor must detect flow through the breathing circuit to set a dose.
	1. **Enter**the prescribed dose in ppm on the electronic keypad. 2. **Press**OK to confirm the entry.	**NOTE** The time to reach target dose may vary up to 10 minutes. If unable to set the dose in Primary Mode, see Troubleshooting, Section 8.7.
		NOTE If manual ventilation is required, proceed to Section 5.4. When adjusting dose, proceed to Section 5.2. If dosing is completed, proceed to Section 6.1.

		**NOTE** The display screen will look as shown after completing steps 1-3. **NOTE** The NO $_2$sensor reading may appear as "—" for the first 30 seconds of dosing while the sample System is preparing.

5.1.2 Setting a Dose when using a Circuit***without***an Adaptive Sensor

This section describes how to set a Nitric Oxide dose when an Adaptive Sensor is not used in the patient circuit, such as when initiating a dose when using a Console as Back-up (Section 5.5). Refer to Section 3.2 for recommended set up diagrams. In the absence of an Adaptive Sensor, the GENOSYL DS will properly deliver and control Nitric Oxide dose. However, the user will have to manually select a Total Flow Range.

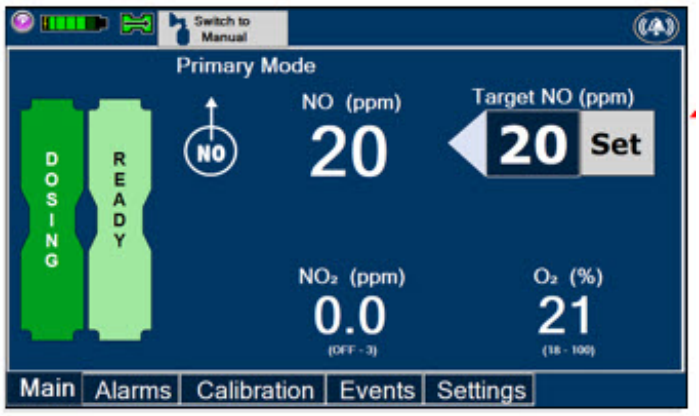
ILLUSTRATION	ACTION	Warnings, Cautions and Notes
	1. **Press**the gray "Set" button on the display screen.	
	1. **Confirm**Total Flow Range is appropriately selected. 2. **Enter**the prescribed dose in ppm on the electronic keypad. 3. **Press**OK to confirm the entry.	**NOTE** The time to reach target dose may vary up to 10 minutes. If unable to set the dose in Primary Mode, see Troubleshooting, Section 8.7.
		NOTE If manual ventilation

		is required, proceed to Section 5.4. When adjusting dose, proceed to Section 5.2. If dosing is completed, proceed to Section 6.1.
		**NOTE** The display screen will look as shown after completing steps 1-3. **NOTE** The NO $_2$sensor reading may appear as "--" for the first 30 seconds of dosing while the sample system is preparing.

5.2 Adjusting the Dose

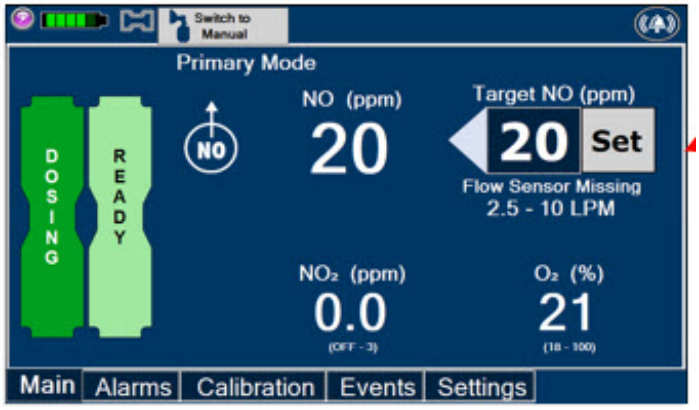
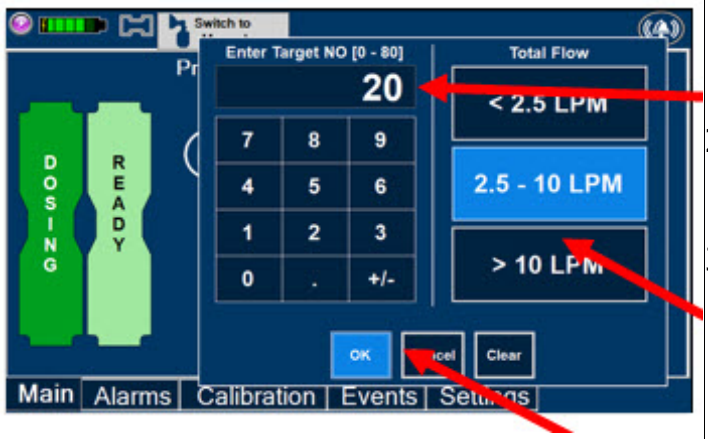
To adjust the dose of Nitric Oxide administered per hospital protocol or physician order, follow the instructions listed below.

5.2.1 Adjusting the Dose when using a Circuit***with***an Adaptive Sensor

ILLUSTRATION	ACTION	Warnings, Cautions and Notes
	1. **Press**the gray "Set" button to access the electronic keypad on the display screen on the Dosing Console.	

	1. **Enter**the prescribed dose using the electronic keypad. 2. **Press**"OK" to confirm the dose and to start dosing administration.	**NOTE** If dosing is complete, proceed to Section 6.

5.2.2 Adjust the Dose and Flow Range when using a Circuit*without*an Adaptive Sensor

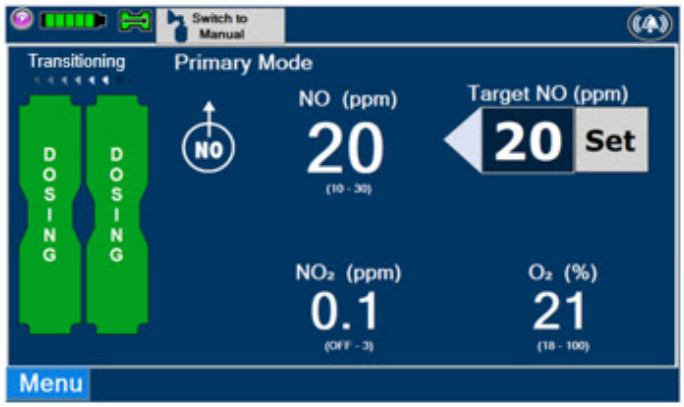
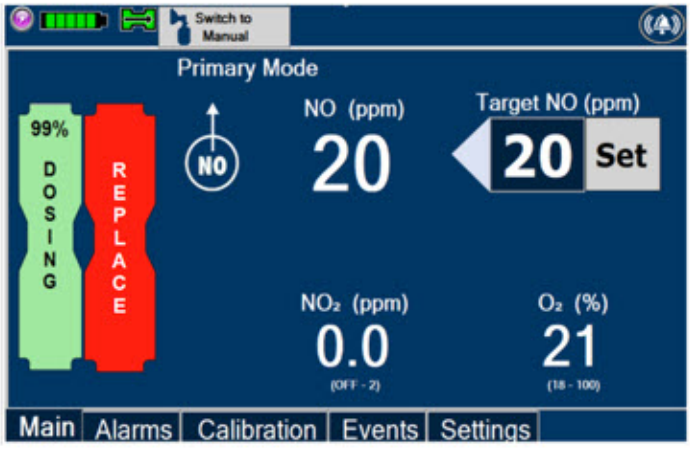
ILLUSTRATION	ACTION	Warnings, Cautions and Notes
	1. **Press**the gray "Set" button to access the electronic keypad on the display screen on the Dosing Console.	
	1. **Enter**the prescribed ppm dose using the numeric keypad. 2. Adjust Total Flow Range, if necessary. 3. **Press**"OK" to confirm the dose and to start dosing administration.	**NOTE** If dosing is complete, proceed to Section 6.

5.3 Replacement of a Depleted Cassette

The GENOSYL DS automatically switches from the dosing Cassette to the secondary Cassette in the Dosing Console once the Cassette is depleted if a secondary Cassette is

properly inserted and preheated. After transition, the depleted Cassette is automatically ejected.

CAUTION
User should always have a secondary Cassette inserted in the Dosing Console and preheated in order for auto transition to occur. User should replace depleted Cassette as soon as possible after ejection.

ILLUSTRATION	ACTION	Warnings, Cautions and Notes
		**NOTE** The Console will automatically transition to the secondary Cassette if properly inserted and preheated. The screen to the left will be displayed during the transition process.
	1. Follow onscreen instructions to replace Cassette.	

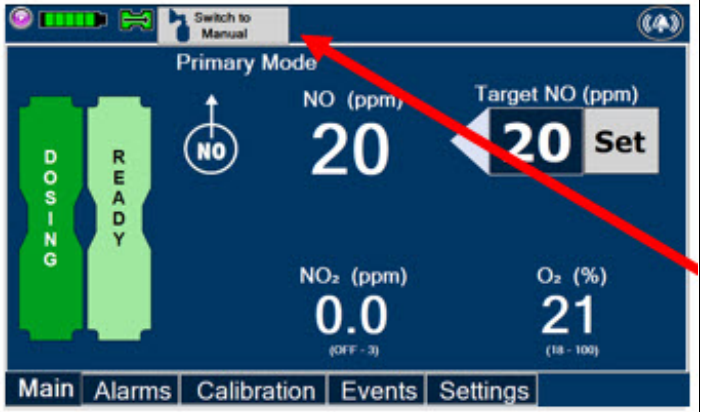
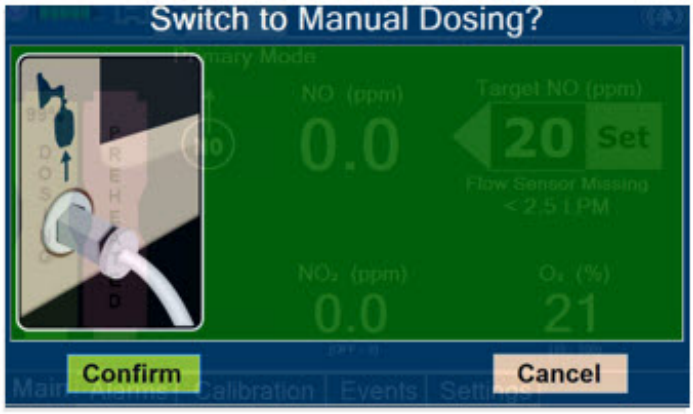
5.4 Manual Mode

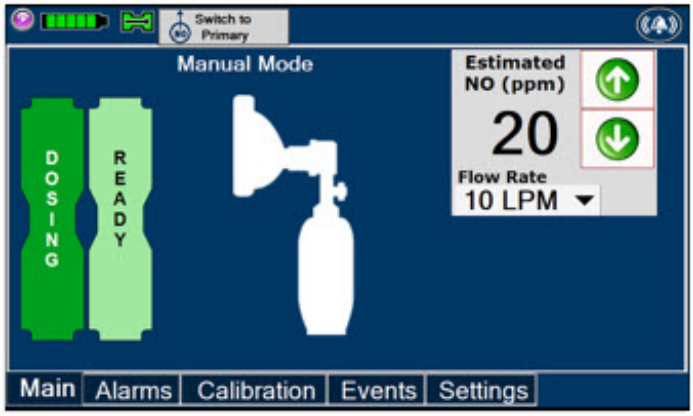
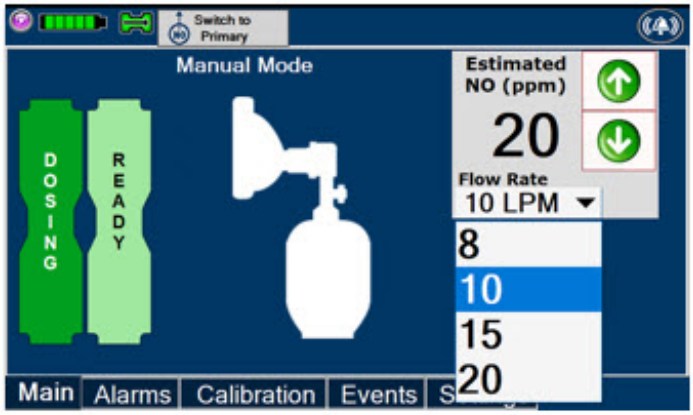
NOTE
• When entering Manual Mode, the set target dose in Primary Mode will carry over to Manual Mode if 5 ppm or greater. Less than 5 ppm set target dose in Primary will default to 5 ppm dose in Manual Mode. However, dose and flow rate may need to be adjusted for specific situations. The GENOSYL DS Smart Feedback System™ is disabled while in Manual Mode. To reinitiate the Smart Feedback System, switch back to Primary Mode as soon as the situation permits. • After a Console is in Manual Mode for more than two minutes, a reminder tone will sound in ten second intervals to alert the user that the Console is still in Manual Mode.

5.4.1 Manual Ventilation Use (Bagging)

This section will describe NO administration when manual ventilation is required.

WARNING
• ALWAYS ensure that the manual flow displayed on the Console matches the flow set into the resuscitation bag. Incorrect flow settings may result in an incorrect estimation of NO delivery. If the flow into the manual equipment is too low, there is risk of overdosing the patient with NO. • ALWAYS squeeze the bag several times, after starting fresh gas flow, to empty residual gas in the bag prior to using the System to ventilate a patient. Failure to do so could result in higher NO_2 levels being delivered to the patient. • ALWAYS use the smallest bag adequate to deliver the desired tidal volume. Failure to do so could result in higher NO_2 levels being delivered to the patient. • ONLY use a manual resuscitation bag with the GENOSYL DS for a short time (e.g., less than one hour) when on battery only. Otherwise, the System may shut off and may result in injury or death.

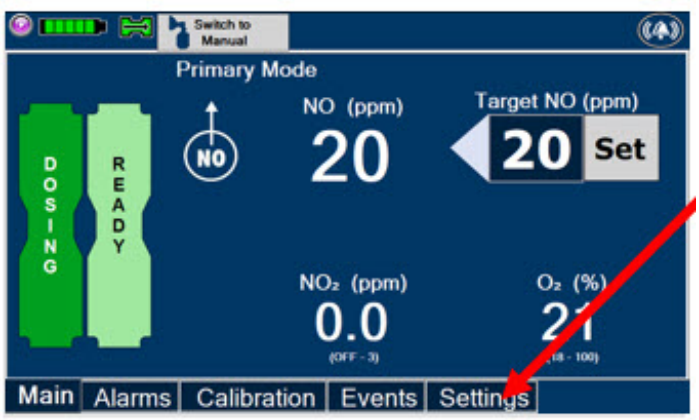
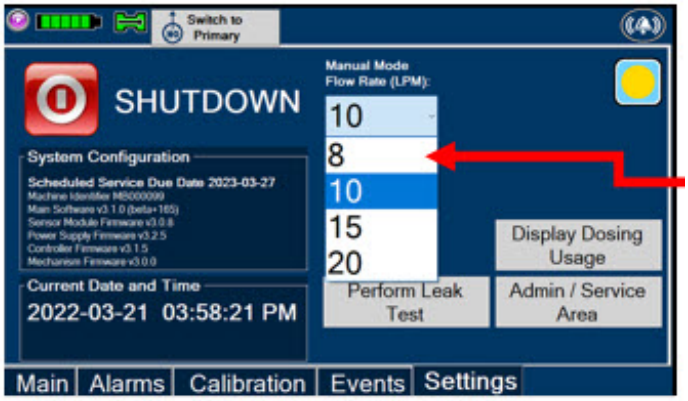
ILLUSTRATION	ACTION	Warnings, Cautions and Notes
	1. **Ensure** the oxygen flow source is set appropriately or adjust as needed. 2. **Press** the button "Switch to Manual" on the Dosing Console.	
	1. **Press** Confirm to switch to Manual Dosing.	**WARNING** If the dilution flow rate displayed on the screen does not match the wall source, then the estimated NO may be inaccurate.
		NOTE Dosing has been initiated at the same dose setting (ppm)

		as in Primary Mode. If the primary dosing was set at "0" prior to pressing the "Switch to Manual" button, the estimated NO will also be at "0" and will need to be adjusted. If the dose was set between 1 and 5 ppm prior to pressing the "Switch to Manual" button, the estimated NO dose will also be at "5 ppm" and may be adjusted.
	1. To **resume**primary dosing, see Section 5.4.3.	**NOTE** If an adjustment of the NO concentration is required, press the green up and down arrows. If an adjustment to the Dilution Flow Rate is required while in Manual Mode, press the LPM value and a drop-down menu will expand. Press the prescribed value. The new value will be highlighted in blue and the drop-down menu will collapse.

5.4.2 Preset Manual Mode Flow Rate (OPTIONAL)

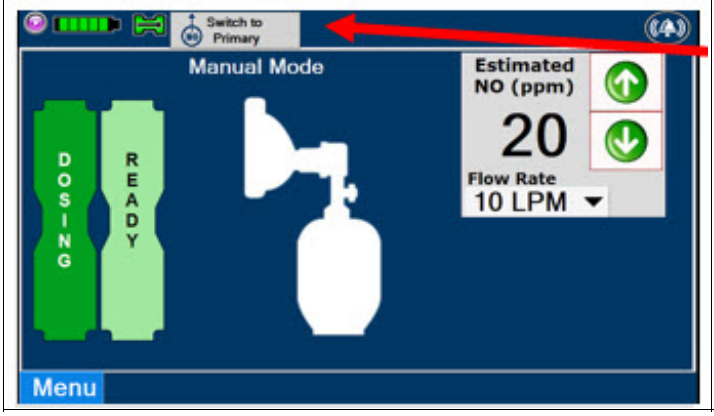
User has the option to preset a Manual Mode Flow rate. This can be completed during set up or at any time.

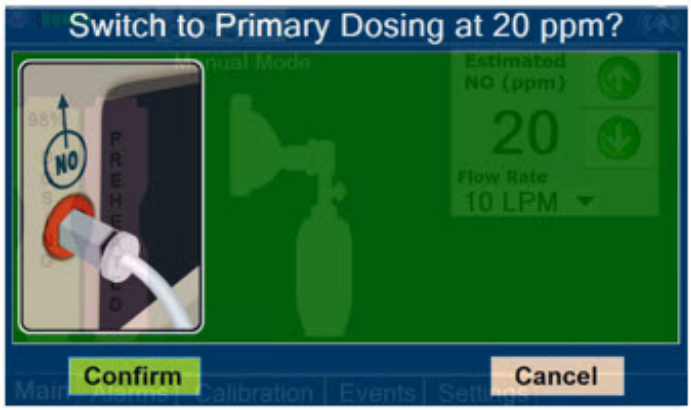
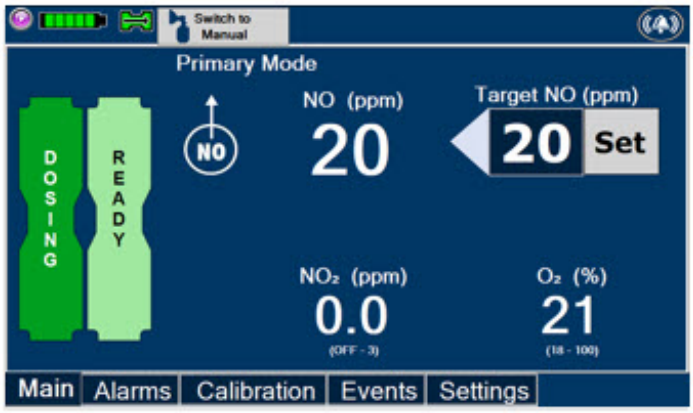
ILLUSTRATION	ACTION	Warnings, Cautions and Notes

	1. Navigate to the Settings Tab.	
	1. **Select**the Flow Rate from the drop-down menu.	**NOTE** The Console will default to a Flow Rate of 10 LPM if not adjusted. Any adjustment will be retained until the Console is powered down.

5.4.3 Resuming Primary Dosing

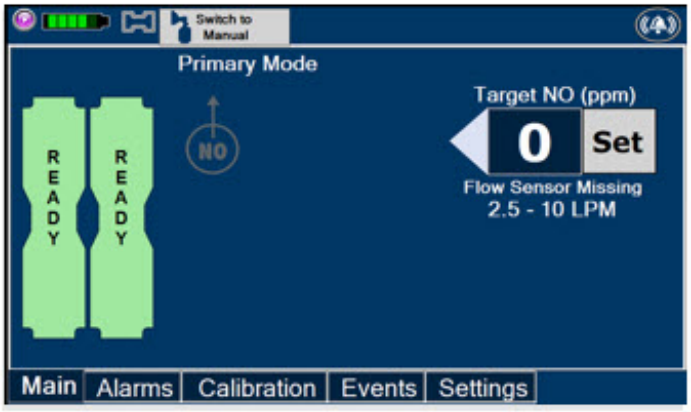
This section describes the process for resuming primary dosing from Manual Mode.

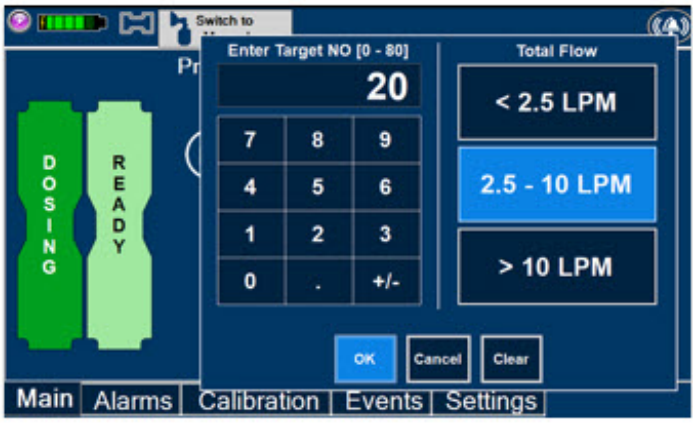
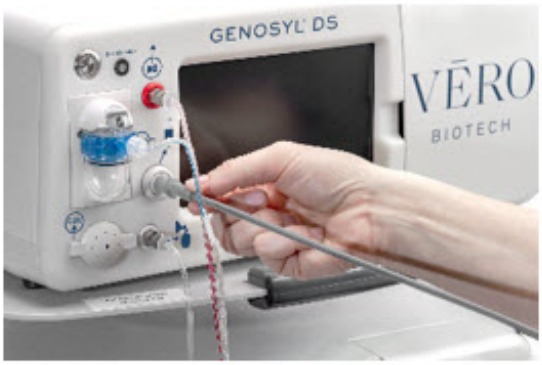
ILLUSTRATION	ACTION	Warnings, Cautions and Notes
	1. **Press**the "Switch to Primary" button at the top of the Manual Mode screen.	

	1. **Press**"Confirm" to start dosing or "Cancel" to cancel.	**NOTE** The NO dose used in Manual Mode will become the set target dose in Primary Mode.
		**NOTE** The display screen will look as shown after completing steps 1-2.

5.5 Console Use as a Back-up

This section describes the process of activating the Cassette in the Back-up Console. Delivery of NO will begin immediately upon Cassette activation.

DISPLAY	ACTION	Warnings, Cautions and Notes
	1. Press the "Set" button on the Back-up Console which will display the NO dose electronic keypad and Flow Selection menu.	
		NOTE The Back-up Console

	1. Confirm Dose and Total Flow range is appropriately selected. 2. Press "OK" to confirm entry	screen will be as shown. The default Total Flow range displayed will be <2.5LPM and the default dose will be 20 ppm unless otherwise selected by the user. See Section 5.1.2 The Back-up Console is now the Dosing Console.
	1. Connect the Adaptive Sensor Cable to the front of the new Dosing Console.	

SECTION 6
CONSOLE SHUTDOWN

6. CONSOLE SHUTDOWN AND CASSETTE DISPOSAL

WARNING
NEVER turn the rear power switch OFF until the System has gone through a controlled shutdown or instructed by VERO Technical Support. Turning the rear power switch OFF prematurely (e.g., while it is still in use) will immediately shut down the device. This may result in interruption in NO delivery to the patient, which may cause injury or death.

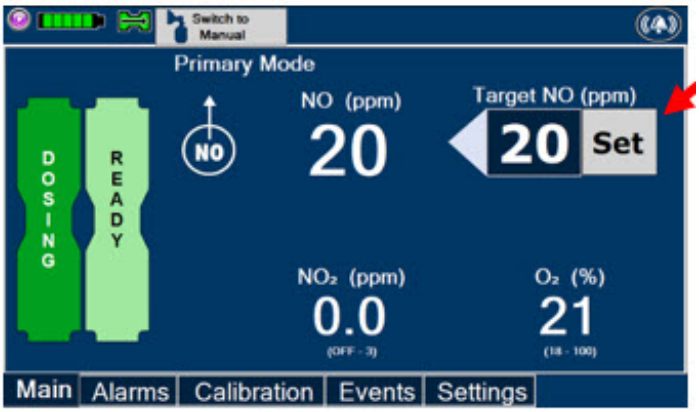
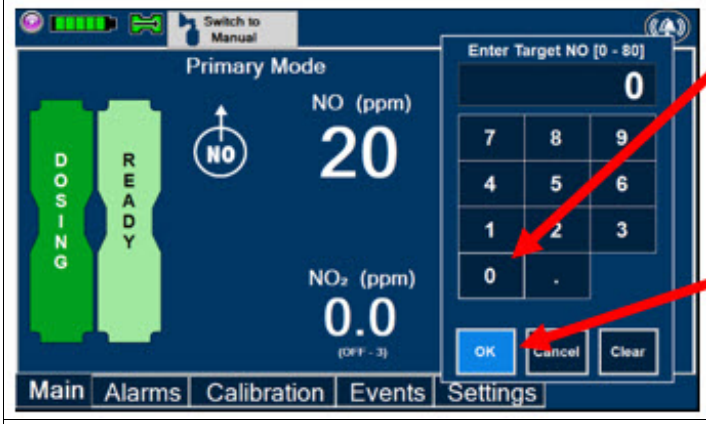
CAUTION
• NEVER turn the rear power switch OFF until the System has gone through a controlled shutdown or instructed by VERO Technical Support. Turning the rear

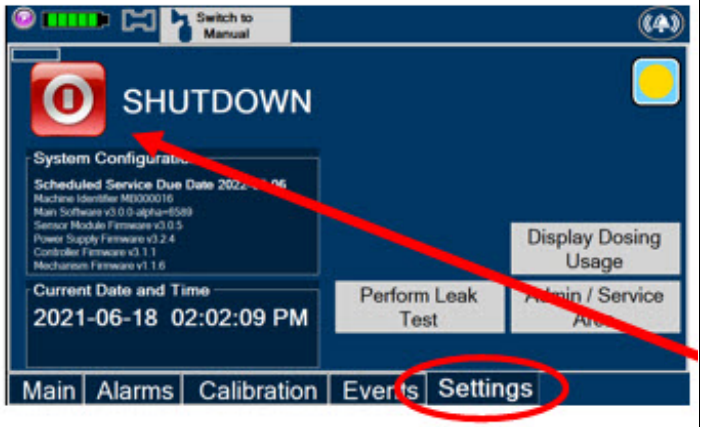
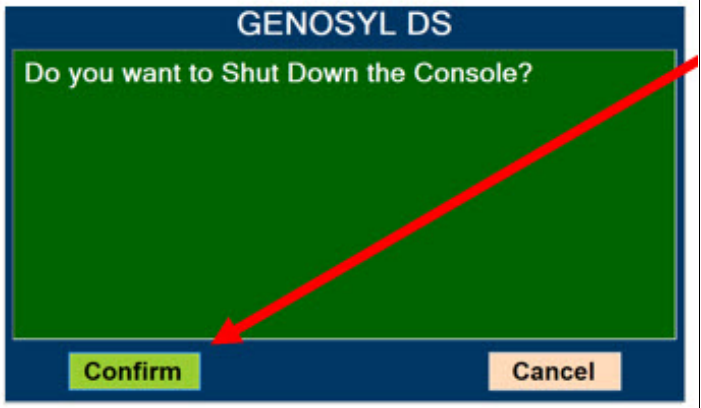
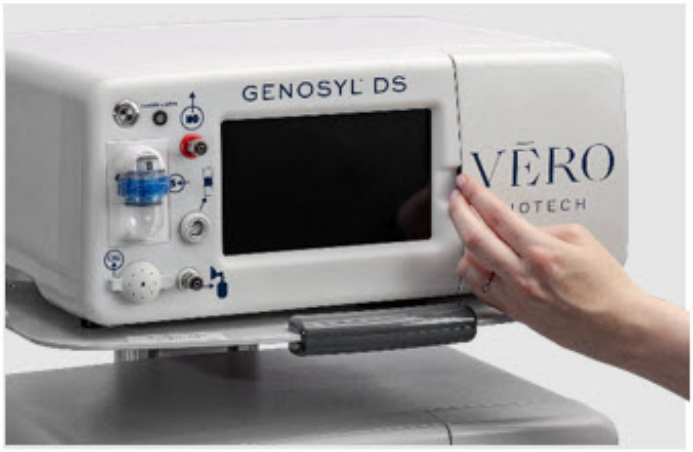
power switch OFF prematurely (e.g., while it is still in use) will immediately shut down the device and may cause improper operation upon restart.
- ALWAYS power down the GENOSYL DS Console and disconnect the power to the Console when not in use. Failure to do so may lead to permanent damage to the Console.

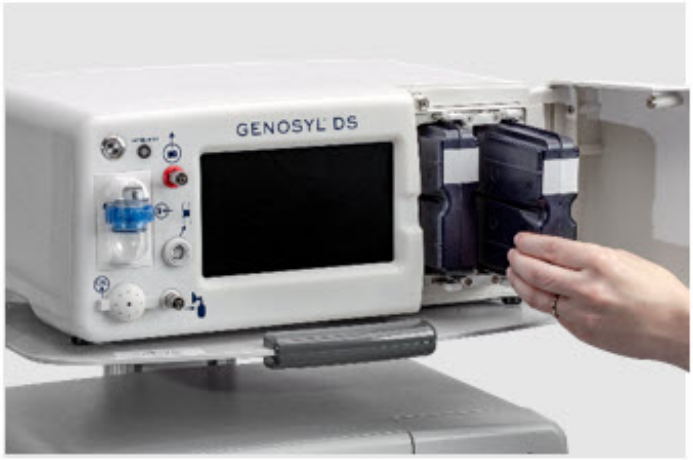
NOTE
It is recommended that the Console be rebooted at least once every 30 days.

6.1 Console Shutdown

If the administration of NO must be stopped, then the dose level must be set to "0". The following procedure describes how to remove the Cassette and the following section will describe how to shut down the Console.

DISPLAY	ACTION	Warnings, Cautions and Notes
	1. **Press**the gray "Set" button to access the electronic keypad on the display screen.	
	1. **Set**the dose to "0" using the electronic keypad. 2. **Press**"OK" to confirm the entry.	

	1. If the Settings Tab is not displayed, **press** the "Menu" tab to access the sub-level tabs. 2. **Press** the "Settings" tab on the display menu. 3. **Press** the red "System Shutdown" icon.	
	1. **Press** "Confirm" to confirm shutdown. 2. **Wait** until the Console shuts down, the display screen appears blank, and the Console emits an audible beep.	**NOTE** If the System does not shut down, see Troubleshooting, Section 8.7.
	1. **Open** the Cassette Access Door.	
		NOTE The Console will inert any remain contents

	1. **Remove**the Cassettes by pulling the Cassette straight out. 2. **Dispose**the inerted Cassettes per hospital policy.	any remain contents from a dosing Cassette upon ejection, rendering it unusable. If a Cassette has only been preheated, and not used for dosing, the contents have not been inerted and it can still be used. The Cassette State Window will remain blue on Cassettes that have not been inerted.
	1. **Press**the Black Rocker Power Switch to the "OFF" position. 2. **Repeat**steps 1-12 for the other Console.	**WARNING** NEVER turn the rear power switch OFF until the System has gone through a controlled shutdown or instructed by VERO Technical Support. Turning the rear power switch OFF prematurely (e.g., while it is still in use) will immediately shut down the device. This may result in interruption in NO delivery to the patient, which may cause injury or death. **CAUTION** NEVER turn the rear power switch OFF until the System has gone through a controlled shutdown or instructed by VERO Technical Support. Turning the rear power switch OFF prematurely (e.g., while it is still in use) will immediately shut down the device and may cause

		improper operation upon restart.

6.2 Cassette Disposal

Following dosing use, any remaining Cassette liquid contents in a dosing Cassette are purged into an inerting chamber that is built into the Cassette, where the contents are chemically neutralized, rendering the Cassette safe for disposal. When the Cassette liquid contents are emptied into the inerting chamber, the Cassette State Window on the front of the Cassette reddens and bleaches from its original blue color, indicating the Cassette is depleted. The Cassette can now be disposed of per hospital policy.

GENOSYL ®DS

SECTION 7
USING THE SYSTEM IN THE MR SCANNER ROOM

7. USING THE SYSTEM IN THE MR SCANNER ROOM

WARNING
• The GENOSYL DS is classified as MR Conditional with MR scanners of 1.5 or 3.0 Tesla strength ONLY in areas where the field strength is less than 100 gauss. • ALWAYS operate at a fringe field of less than 100 gauss. This device contains ferromagnetic components and may experience strong attraction close to the magnet. • DO NOT exceed 100 gauss; System operation may be impacted. Confirm Cart caster lock function. Optionally connect tether. • NEVER use the GENOSYL DS in the MR scanner room without gauss alarms installed. • ALWAYS verify at least one gauss alarm is functioning properly prior to use in the MR environment. • DO NOT use the GENOSYL DS in the MR environment if neither gauss alarm is functional. • ALWAYS move System away from the MR scanner if the gauss alarm sounds. The gauss alarm will sound if the System is too close to the MR scanner. Move System away from the MR scanner until the gauss alarm stops sounding. • ALWAYS verify that the GENOSYL DS Cart casters are locked after positioning the System in the MR scanner room. • ALWAYS verify that the GENOSYL DS is securely attached to the Cart. • ALWAYS arrange power cord, MR patient gas sample line, and NO delivery line to avoid entanglement, strangulation and/or a trip hazard. • DO NOT use the GENOSYL DS in the MR environment if the Cart moves when the brake caster locks are engaged. • NEVER perform NO or NO_2 calibration within the MR scanner room. Calibration equipment is a potential projectile hazard.

NOTE
Refer to Section 11.5 for MR Signal-to-Noise Ratio and Artifact Dimension Analysis

7.1 Connection to the Ventilator Breathing Circuit

To connect the GENOSYL DS to an MR Conditional ventilator, see Section 3.2for example breathing circuits. When using the GENOSYL DS in the MR environment, a Sample Line Extension may be required. See Section 3.5.2for steps to install the Sample Line Extension.

NOTE
• Connections to various ventilators are unique to each manufacturer as well as their corresponding disposable circuits. • A Sample Gas Line Extension may be required. Refer to Section 3.5.2 for instructions to install a Sample Gas Line Extension

7.2 Transferring to and from the MR Scanner Room

WARNING
• NEVER use the GENOSYL DS in the MR scanner room without gauss alarms installed. • DO NOT use the GENOSYL DS in the MR environment if neither gauss alarm is functional. • ALWAYS verify at least one gauss alarm is functioning properly prior to use in the MR environment. • ALWAYS verify that the GENOSYL DS is securely attached to the Cart. • NEVER perform NO or NO_2 calibration within the MR scanner room. Calibration equipment is a potential projectile hazard.

1. Verify that both gauss alarms are installed on the GENOSYL DS Cart.

2. Move the patient, MR conditional ventilator circuit, and GENOSYL DS into the MR scanner room.

3. Position the GENOSYL DS outside of the MR exclusion zone, as shown in Figure 22.

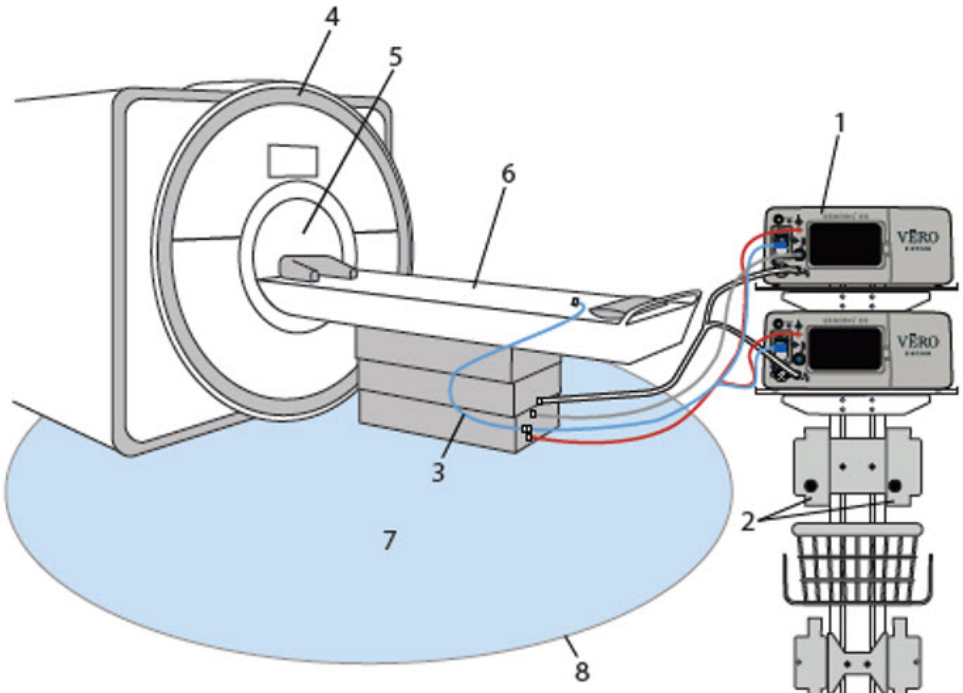
WARNING
ALWAYS move System away from the MR scanner if the gauss alarm sounds. The gauss alarm will sound if the System is too close to the MR scanner. Move System away from the MR scanner until the gauss alarm stops sounding.

4. Engage the locks on wheels and confirm caster lock function. Attaching a facility supplied tether to the System Cart handle may be utilized as a redundant means to limit the distance the Cart can move.

WARNING
• ALWAYS verify that the GENOSYL DS Cart casters are locked after positioning the System in the MR scanner room. • DO NOT use the GENOSYL DS in the MR environment if the Cart moves when the brake caster locks are engaged.

5. Move the patient, MR conditional ventilator, and GENOSYL DS outside of the MR scanner room.

6. Verify ventilator and GENOSYL DS function following transition from the MR scanner room.



1. GENOSYL® Delivery System
2. Gauss Alert
3. Sample Line Extension
4. MR Scanner
5. MR Scanner Bore
6. Patient Table
7. Exclusion Zone (actual shape may vary)
8. 100 Gauss Line

Figure 22: MR Scanner Room

GENOSYL ®DS

SECTION 8
ALARMS, ALERTS, AND TROUBLESHOOTING

8. ALARMS, ALERTS, AND TROUBLESHOOTING

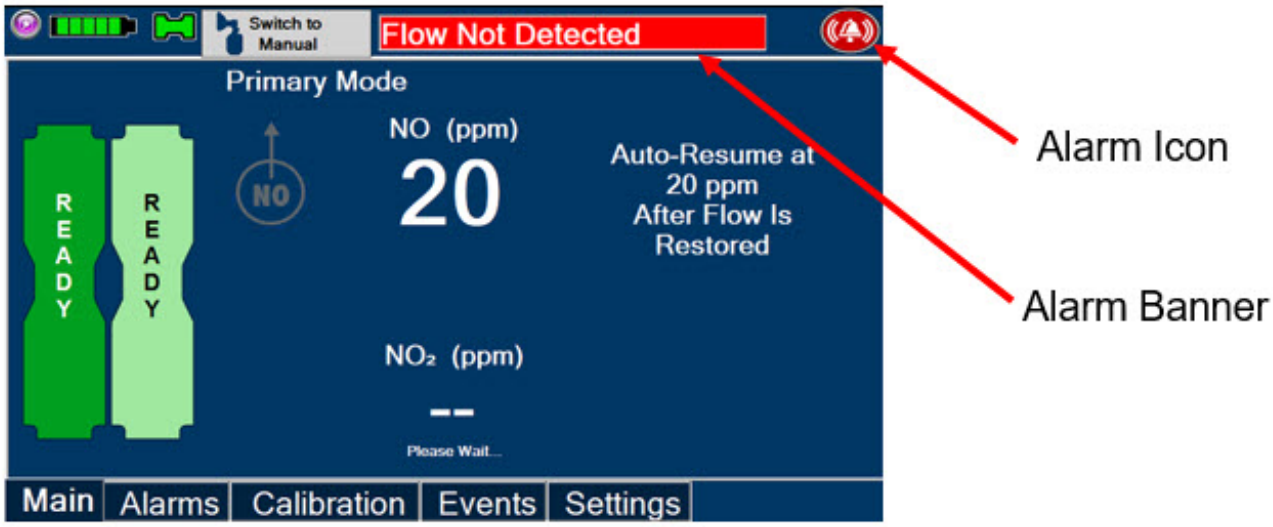
WARNING
ALWAYS ensure patient safety before troubleshooting (such as an activated alarm) or replacing a problematic item. Not monitoring the patient prior to attending to an alarm can result in injury or death.

8.1 Alarms, Alerts, and Troubleshooting

This section contains the System alarms and messageS in order of High (red), Medium (yellow), and Low Priority (cyan) followed by Informational Messages (green). The table shows the alarm/symptom, the possible cause(s) of the alarm and recommended action

to resolve the alarm. If the alarm/issue cannot be resolved, contact Technical Support at **877-337-4118**.

A sample screen with an active alarm is shown below:



The alarm banner contains a drop-down menu containing a list of all alarms should there be multiple activated. The alarm icon is always present on the top right of the screen and tapping the icon will pre-silence or silence alarms. Refer the table below for descriptions of each alarm status:

Table 3: Alarm Icon Descriptions

ALARM ICON DISPLAY	DESCRIPTION
	No active alarm condition is detected on the Console. Tap this icon to activate the Pre-Silence feature.
	Alarms are actively pre-silenced. Countdown of time remaining appears under the icon. Pre-silence lasts for 120 seconds. Low/High NO, High NO_2, Low/High O_2, Water Trap Removed, and Dosing Cassette Removed alarms are pre-silenced. Alarms will still be visible on alarm banner but audible alarm will not sound.
	Console has an active alarm condition that requires attention. Tap the icon to silence the alarm for 120 seconds.
	Console has an active alarm condition that requires attention and the alarms have been silenced. Countdown of time remaining for silence appears on bottom of icon.

The alarm order, color, and audio signal will follow the highest priority alarm.

Table 4: Alarm Characteristics

Alarm Priority	Color	Flashing Frequency	Flashing Duty Cycle	Sound Level
High	Red	1.4 to 2.8 Hz	40-60%	79.8 dBA
Medium	Yellow	0.4 to 0.8 Hz	40-60%	76.1 dBA
Low	Cyan	Constant (on)	100%	63.3 dBA

Some alarms may be adjusted within the Alarms Tab. See Table 5below for adjustment characteristics. The System will always resort to the original default alarm settings upon reboot or complete power failure.

In addition, the System has a fallback safety dose interruption feature which will temporarily interrupt delivery of NO when the sensors detect a sampled value of ≥ 100 ppm NO and/or ≥ 3 ppm NO_2. The System will resume NO dosing after dissipation of high gases without operator input.

Review Table 5for complete details about the alarm adjustment ranges, defaults, alarm activation timing and interruption conditions.

Table 5: Alarm Ranges, Defaults and Dose Interruption Condition

Alarm	Adjustment Range	Default Setting	Alarm Activation	Interruption Condition
High NO (ppm)	0 – 100 ppm	+ 50% of set value or 2 ppm (Whichever is greater)	10 minutes after dose >0 ppm entered	≥ 100 ppm
Low NO (ppm)	0 – 99 ppm	- 50% of set point or 2 ppm (Whichever is greater)	10 minutes after dose >0 ppm entered	NA
High NO_2(ppm)	1-2.9 ppm	3 ppm	30 seconds after dose > 0 ppm entered	≥ 3 ppm
High O_2(% v/v)	22 – 100 ppm	100 ppm	Immediately after dose > 0 ppm entered	N/A
Low O_2(% v/v)	18 – 99 ppm	18 ppm	Immediately after dose > 0 PPM entered	N/A

NOTE
The safety dose interruption feature is active immediately upon setting a dose greater than 0 ppm. The NO and NO_2alarms do not need to be active for the safety dose interruption feature to be activated.

Alarms are legible for a person with 20/20 vision at a distance of 1 meter when viewed directly on the screen.

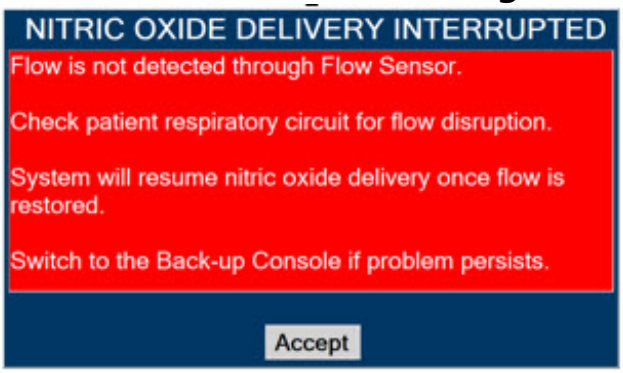
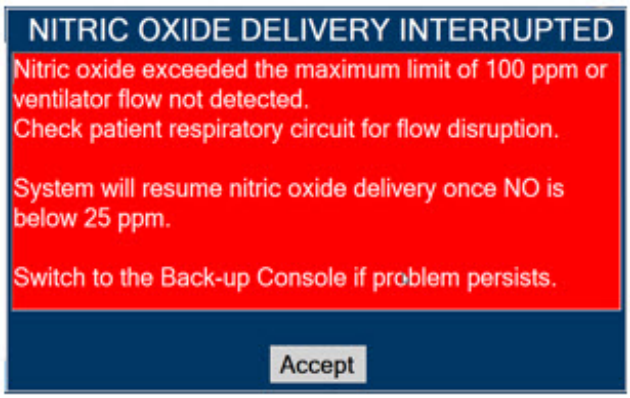
An alarm history indicating the date, time, and type of alarm can be viewed by selecting the Alarms Tab and then selecting the alarms history button. The alarm history can be cleared by pressing the "Clear Alarm Button". If the alarm history reaches capacity, the

oldest alarms will begin rolling off and become non-visible to the user. Upon Console shut down or power loss, the alarm log is cleared. If the alarm log is cleared, or reaches capacity, history of alarms will still be recorded in permanent memory accessible when logged in as admin. The operator of the equipment should be physically in front of the Console while interacting with the System. During NO delivery, the operator should remain within visual and auditory distance of the System.

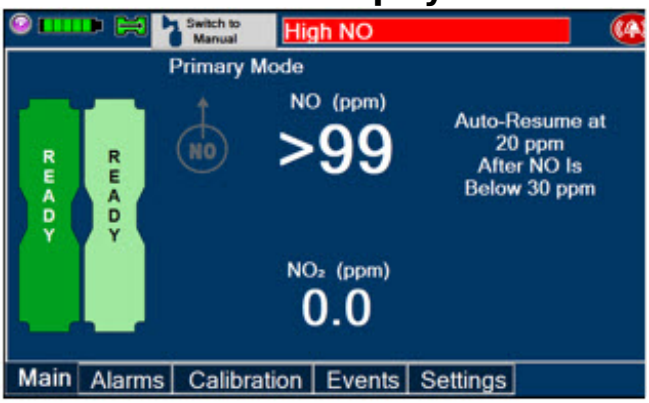
The alarm system is automatically tested during the initial power-on self-test with an audible beep to confirm successful completion. Should there be an issue with communication to the alarms System electronics, a Hardware Failure error message will appear at the end of the self-test.

8.2 High Priority Alarms and Messages

High priority alarms and messages will have a red background and be accompanied by an audible alarm. These alarms and messages require immediate operator response.

High Priority Alarms and Messages		
Alarm/Symptom	**Possible Cause**	**Recommended Action**
Nitric Oxide Delivery Interruption due to Flow Not Detected Message Box:  **Banner:** 	• Adaptive Sensor not detecting flow • Cause not determined	Once flow is detected through the Adaptive Sensor, dosing will resume automatically and this fallback mode will be cancelled. 1. Verify proper connection of Adaptive Sensor to respiratory circuit 2. Verify flow is present in the respiratory circuit
Nitric Oxide Delivery Interruption due to High NO Message Box:  **Banner:**	• Flow changed abruptly in	This fallback mode will be cancelled once the nitric oxide level drops below the set dose + 20%. 1. Verify flow is present in the patient's respiratory circuit. 2. Allow time for the sensor measurement to adjust while

Screen Display:

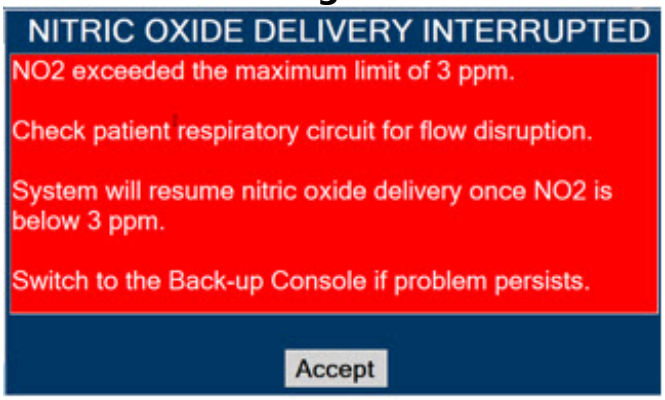


respiratory circuit
- Low or no flow in patient respiratory circuit
- Cause not determined

completing the next steps.
3. Verify GENOSYL DS gas line connections are tight by loosening then retightening each connection on the red injection and blue sample lines.
4. If the sensor measurement does not adjust, switch to Back-up Console.
5. Call Technical Support.

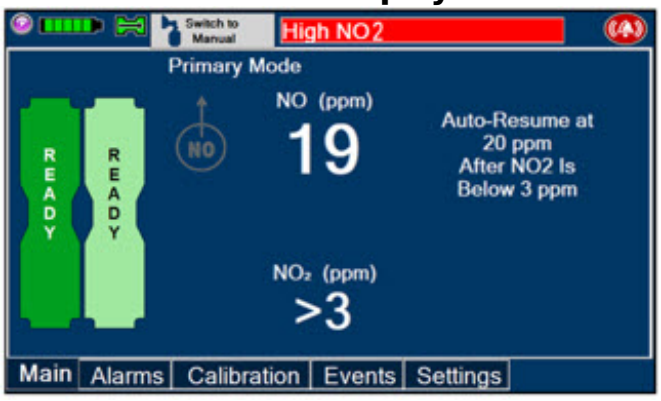
Nitric Oxide Delivery Interruption due to High NO 2

Message Box:



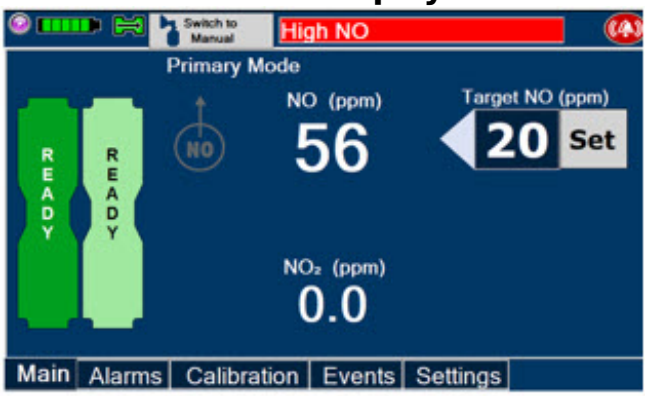
Banner:

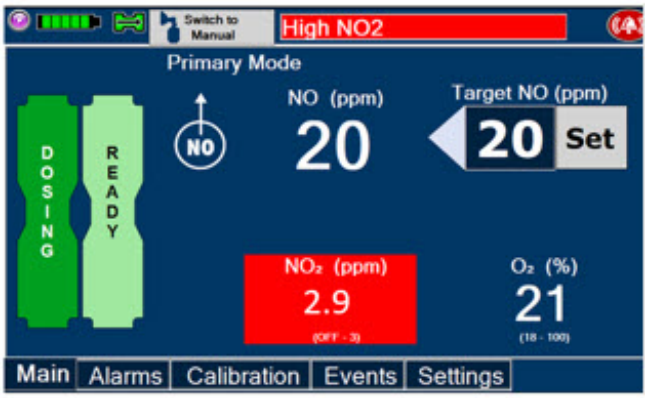
Screen Display:



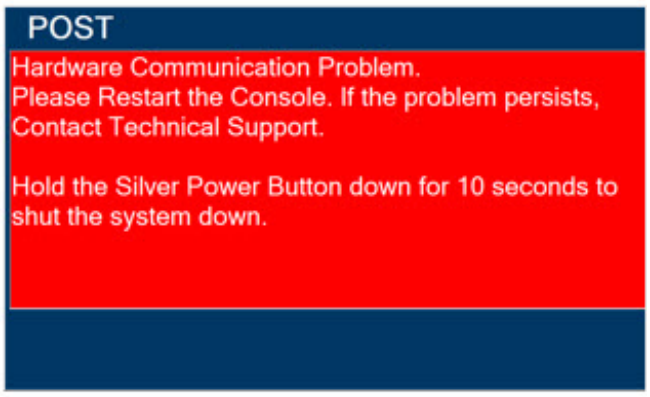
- Low or no flow in patient respiratory circuit
- Respiratory flow changed abruptly
- Leak in patient respiratory circuit
- Cause not determined

This fallback mode will be cancelled once the NO2 level drops below 3 ppm.
1. Ensure flow from patient's respiratory device.
2. Allow time for the sensor measurement to adjust while completing the next steps.
3. Verify GENOSYL DS gas line connections are tight by loosening then retightening each connection on the red injection and blue sample lines.
4. If the sensor measurement does not adjust, switch to Back-up Console.
5. Call Technical Support.

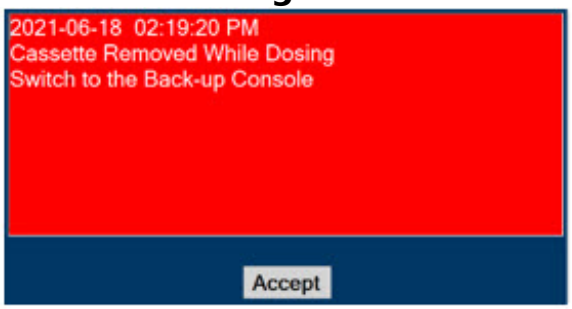
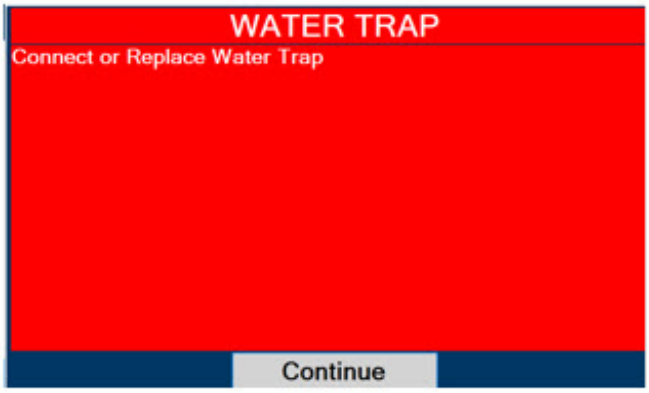
High NO Alarm Message Box: None **Banner:**  **Screen Display:**  	• Respiratory circuit flow changed abruptly • Low or no flow in patient respiratory circuit • High NO alarm may be inappropriately set • Cause not determined	1. Verify flow is present in the patient's respiratory circuit. 2. Allow time for the sensor measurement to adjust while completing the next steps. 3. Verify GENOSYL DS gas line connections are tight by loosening then retightening each connection on the red injection and blue sample lines. 4. Go to the Alarms screen and check the NO alarm setting. Set alarm to the desired setting. 5. If the sensor measurement does not adjust, switch to Back-up Console. 6. Call Technical Support.
High NO $_2$Alarm Message Box: None **Banner:**  **Screen Display:**	• Low or no flow in patient respiratory circuit	1. Verify flow is present in the patient's respiratory circuit. 2. Allow time for the sensor measurement to adjust while completing the next steps. 3. Verify GENOSYL DS gas line connections are tight by loosening

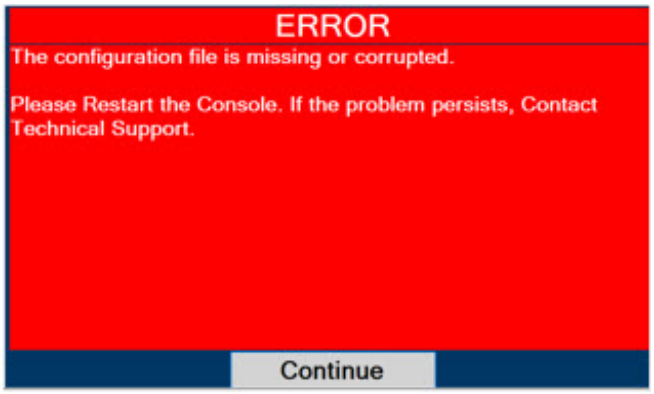
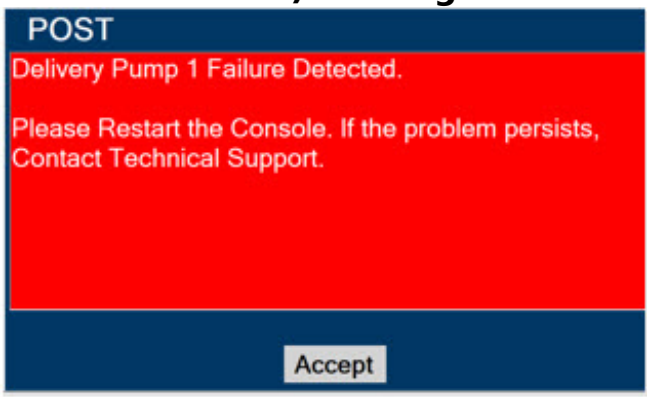
	• Ventilator flow changed abruptly • High NO $_2$alarm may be inappropriately set • Cause not determined	then retightening each connection on the red injection and blue sample lines. 4. Go to the Alarms screen and check the NO $_2$alarm setting. Set alarm to the desired setting. 5. If the sensor measurement does not adjust, switch to Back-up Console 6. Call Technical Support
Low NO alarm Message Box: None	• Gas lines are not connected or properly placed in the respiratory circuit • Water Trap full • Leak in respiratory circuit • Alarm limit not	1. Verify GENOSYL DS gas line connections are tight by loosening then retightening each connection on the red injection and blue sample lines. 2. Ensure gas sample tee is placed 6 to 12 inches from the patient wye adapter. 3. Check the respiratory circuit for the presence of leaks. 4. If not using an Adaptive Sensor, confirm total flow range is properly selected. 5. Allow time for the sensor measurement to adjust while completing the next steps. 6. Empty Water

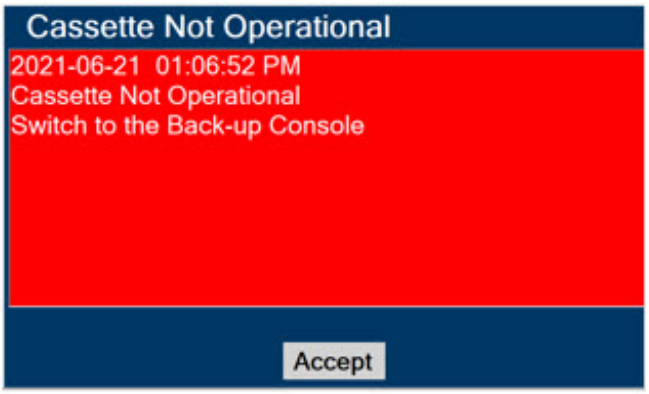
Banner:  	adjusted properly • NO Cassette needs to be replaced • Cassette is depleted without a second Cassette inserted • Gas sample tee placed too close to patient wye adapter • Cause not determined	Trap. Replace Water Trap if necessary. 7. If Cassette is depleted, insert a second Cassette if not already present. If auto transition does not occur, switch to Back-up. 8. Ensure dose and flow are set within specifications. (see Section 10.1.4Liters per minute multiplied by ppm should not exceed 800. (Example 40 LPM x 20ppm = 800) 9. Go to alarms screen and check the NO alarm setting. Set the alarm to the desired setting. 10. If sensor measurement does not adjust, switch over to Back-up Console. 11. Call Technical Support.
Calibration Required Message Box: None **Banner:**  	• Calibration for the sensor is required	This fallback mode will be cancelled once a successful high gas calibration has been completed. 1. Calibrate Console (see Section 9.1). 2. If the calibration required alarm occurs after a successful calibration has been completed, call Technical Support.

Hardware Failure Message Box:  **Banner:**  	• Internal hardware damage or communication failure	In this fallback mode, the Console will continue delivering nitric oxide in an open loop mode at the last entered dose. 1. Switch to Back-up Console. 2. Call Technical Support.
Hardware Failure – Power Board Message Box:  **Banner:**  	• Internal hardware damage or communication failure	1. Switch to Back-up Console. 2. Call Technical Support.
Hardware Error During POST (Power On Self-Test) Message Box:  	• Problem occurring during boot-up sequence • Internal hardware damage or communication failure	1. Use other Console if NO delivery is needed immediately. 2. Re-boot by holding Silver Power Button down for 10 seconds. 3. If error message continues, call Technical Support.
Battery Error Message Box: None	• Internal battery error or battery fails to charge	1. Plug in AC power. 2. Verify power connections on Console, power adapters, and AC power source. 3. If error persists

Banner: 	fails to charge • Battery becomes disconnected	and not dosing, re-start Console. 4. If alarm does not clear, switch to Back-up Console and call Technical Support
Line Occlusion (Sample) Message Box: None **Banner:** 	• Stopcock valve on the Sample Line (blue) is in the closed position • Water Trap is full • Blue Sample Line is kinked or occluded • Cause not determined	In this fallback mode, the Console will continue delivering nitric oxide in an open loop mode at the last commanded dose until the line occlusion is resolved. 1. Ensure blue Sample Line Stopcock is in the open position. 2. Empty Water Tap. 3. If occlusion persists after emptying, replace Water Trap. 4. Inspect entire length of blue sample line for kinks or occlusions. 5. Replace gas lines if kink or occlusion cannot be resolved. 6. If issue is still not resolved, switch over to Back-up Console. 7. Call Technical Support.
Line Occlusion (Cal) Message Box: None	• Potential obstruction to calibration port • Calibration tank valve closed during	1. Ensure calibration port is free of debris or damage and nothing is connected. 2. Perform high calibration by following

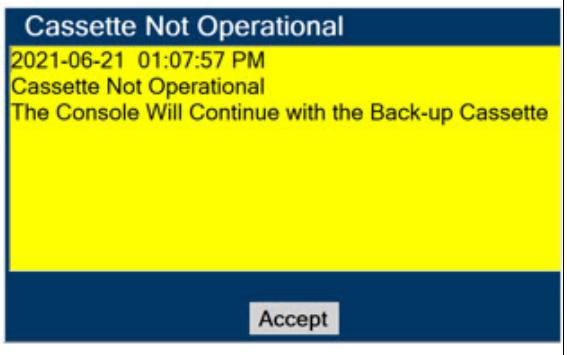
Banner: 	valve closed during high calibration procedure • Cause not determined	procedure in Section 9.1 3. If issue is still not resolved, switch over to Back-up Console. 4. Call Technical Support
Cassette Removed while dosing Message Box:  **Banner:** None	• Cassette manually ejected using emergency ejection tabs • Hardware damage which causes the System to not be able to detect the Cassette • Cause not determined	1. If secondary Cassette is not inserted, transition to Back-up Console 2. Call Technical Support.
Water Trap Not Detected Message Box:  **Banner:** 	• Water Trap not seated properly • Water Trap not present • Cause not determined	In this fallback mode, the console will continue delivering nitric oxide in an open loop mode at the last commanded dose until the water trap is replaced and the leak check is passed. 1. Re-seat Water Trap. 2. Insert new Water Trap. 3. Switch over to Back-up Console. 4. Call Technical Support.
Configuration Parameters Incorrect Message Box:		

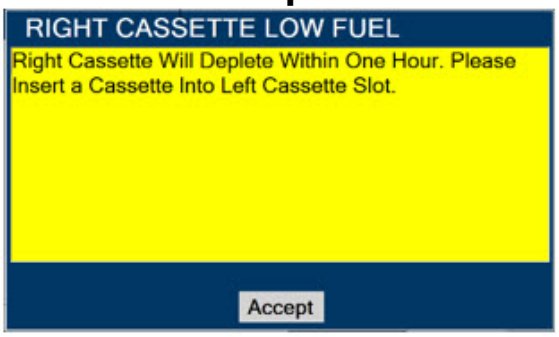
	• File integrity issue	1. Use other Console if NO delivery is needed immediately. 2. Call Technical Support.
Battery Not Detected during POST (Power On Self- Test) Message Box: 	• Battery is not connected properly or not operational	1. Use other Console if NO delivery is needed immediately. 2. Call Technical Support.
Hardware Error During POST (Power On Self-Test) Message Box:  **Banner:** 	• Hardware failure occurred	1. Use other Console if NO delivery is needed immediately. 2. Call Technical Support.
Cassette Not Operational Message Box:		If a secondary Cassette is inserted in the other slot, the Console will automatically switch to the secondary Cassette in this fallback mode.

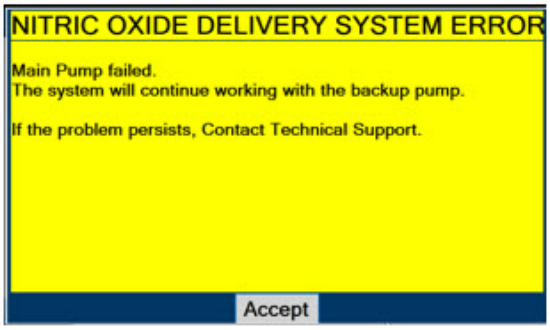
	• Hardware failure within Cassette during dosing	1. If a secondary Cassette is not inserted in the other slot, switch to Back-up Console. 2. Replace Cassette in original Dosing Console 3. If issue is not resolved, switch to Back-up Console. 4. Call Technical Support.

8.3 Medium Priority Alarms and Messages

Medium priority alarms and messages will have a yellow background. Medium priority alarms and messages require a prompt response from the operator.

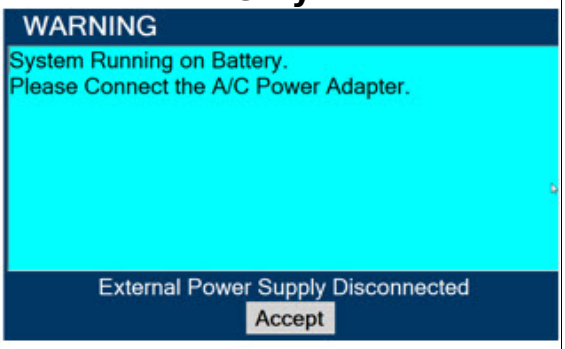
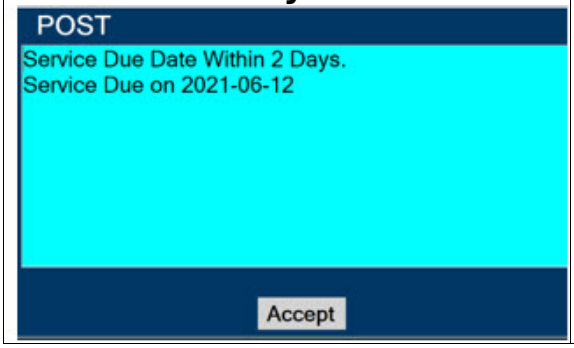
Medium Priority Alarms and Messages		
Alarm/Message	**Possible Cause**	**Recommended Action**
Low Battery Alarm Message box: None Banner: 	• Battery is low	1. Verify power connections on console, power adapters, and AC power source. 2. If AC power is not available, switch to Back- up Console. 3. Then plug into AC power as soon as possible.
Cassette Failure Alarm 	• Internal Cassette issue	1. Replace with a new Cassette. 2. If unresolved, switch to Back-up Console and call Technical Support.
Service Due Date Expired		

	• Scheduled yearly Service date is past due	1. Accept message. 2. Call Technical Support to service System.
Cassette to Expire in 1 Hour 	• Cassette will deplete in 1 hour	1. Ensure secondary Cassette is inserted and ready. 2. Replace Cassette once transition is complete.
Low O_2 Message box: none Banner: 	• Respiratory device setting is incorrect • Alarm setting is incorrect • Ventilator flow is too low	1. Verify respiratory device setting is correct. 2. Set the alarm ranges to the correct setting. 3. Calibrate Console (see Section 9.1). 4. If sensor measurement does not adjust, switch over to Back-up Console. 5. Call Technical Support.
High O2 Message Box: none Banner: 	• Respiratory device setting is incorrect • Alarm setting is incorrect	1. Verify respiratory device setting is correct. 2. Set the alarm ranges to the correct setting. 3. Calibrate Console (see Section 9.1). 4. If sensor measurement does not adjust, switch over to Back-up Console. 5. Call Technical Support.
Delivery Flow Error Message Box:	• Red injection line is kinked	1. Inspect entire length of red injection line for kinks and

 Banner: 	line is kinked or occluded • Kink or occlusion in respiratory circuit • NO port is occluded • Hardware issue caused a failure	occlusions. 2. Insect respiratory circuit for kinks or occlusions 3. Inspect NO output port on front of console for debris or damage. 4. Ensure the air intake is not blocked. 5. Resolve the kink or blockage. 6. If problem persists, call Technical Support.

8.4 Low Priority Alarms and Messages

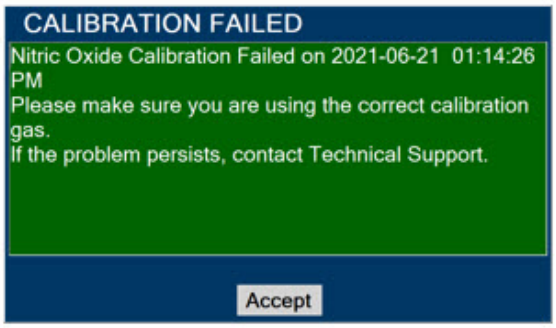
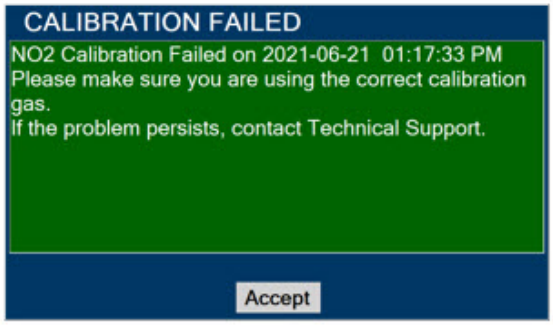
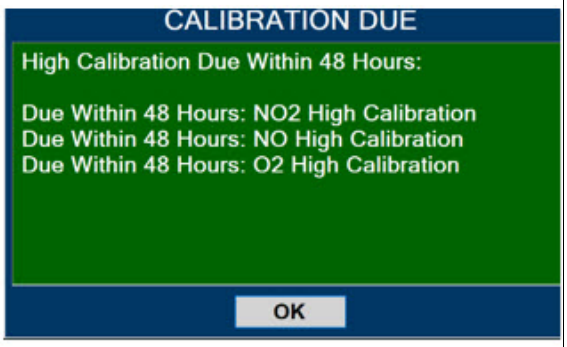
A low priority message will have a turquoise background. A low priority message will require that the operator is aware of the condition.

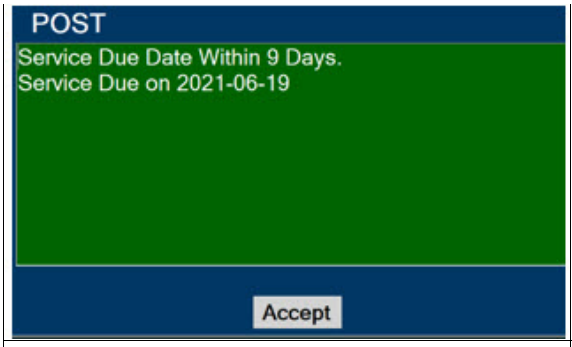
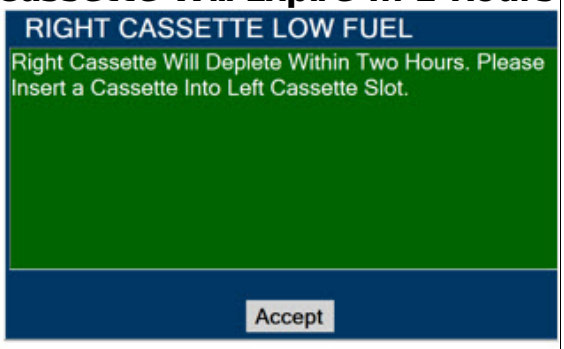
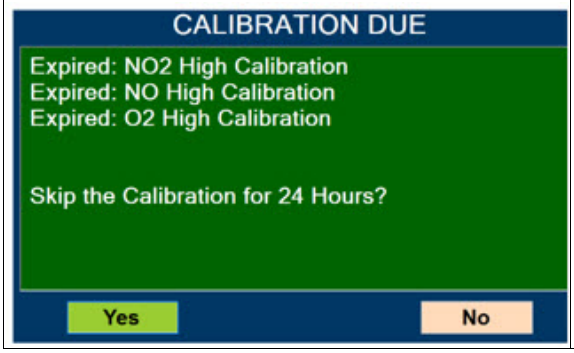
Low Priority Messages and Alarms		
Message/Alarm	**Possible Cause**	**Recommended Action**
System Running on Battery Only 	• AC power is not connected	1. Check the AC power connection. 2. Verify power connections on Console, power adapters, and AC power source. 3. If connecting to AC power does not resolve issue, switch to Back-up Console and call Technical Support.
Service Due Date Within 2 Days 	• Service date is scheduled within 2 days	1. Accept message. 2. Contact Technical Support to have System serviced at earliest convenience.

8.5 Informational Messages

Informational messages will have a green background. These messages require that the user is notified of the condition.

Informational Messages

Message/Alarm	Possible Cause	Recommended Action
System has not Completed Calibration   	• Calibration was not completed • Wrong/empty calibration gas tank used • Calibration tubing is incorrectly connected to the sample port • Failed Gas Sensor	1. Accept message. 2. Obtain correct/full calibration gas tank. 3. Connect calibration tubing to Cal port. 4. Perform gas calibration. See Calibration Section 9.1. 5. If you continue to have problems, call Technical Support.
Calibration Due within 48 Hours 	• Calibration is required within 48 hours	1. Accept message. 2. Perform gas calibration if desired. See Calibration Section 9.1.
Service Due Date Within 14 Days		

	• Service date is scheduled within • 14 days	1. Accept message. 2. Contact Technical Support to have System serviced at your convenience.
Cassette Will Expire In 2 Hours 	• Cassette will expire within 2 hours and no secondary Cassette inserted	1. Insert secondary Cassette. 2. Replace Cassette once transition is complete.
Calibration Due 	• Calibration due date has passed	1. Perform gas calibration. See Calibration Section 9.1.

8.6 GaussAlert™ Alarm

The gauss alarm will sound if the GENOSYL DS is too close to the MR Scanner. If the gauss alarm sounds, move the GENOSYL DS away from the MR scanner until the gauss alarm stops sounding.

WARNING
ALWAYS move System away from the MR scanner if the gauss alarm sounds. The gauss alarm will sound if the System is too close to the MR scanner. Move System away from the MR scanner until the gauss alarm stops sounding.

8.7 Troubleshooting

The table below provides resolutions to issues that may be encountered with the GENOSYL DS.

Issue/Symptom	Possible Cause	Recommend Action
		1. Ensure power is properly connected in the back of

Screen does not turn on	• Battery discharged and not connected to AC power • Screen malfunction	the unit and the wall outlet. Green light on power supply should be on. 2. Ensure battery is connected properly. 3. Wait for System to charge. 4. Power on System. 5. If not resolved, switch to Back-up Console and call Technical Support.
Cassette does not insert properly within Console	• Drop or other physical damage	1. Discard damaged NO Cassette and replace with new Cassette. 2. If new Cassette does not insert properly, switch to Back-up Console and call Technical Support.
Cassette State Window is not blue	• Drop or other physical damage • Cassette was previously activated	1. Discard damaged Cassette and replace with new Cassette.
Pumps are louder than normal	• Enclosure damage • Pump malfunction	1. Call Technical Support.
Cannot set dose in Primary Mode	• Flow not detected through Adaptive Sensor • Water Trap/ Sample Line Leak Test was not performed • Calibration is required for at least one sensor	1. Verify flow is present in patient circuit. 2. Perform Water Trap/ Sample Line Leak Test if not already performed. 3. Perform calibration if required. 4. If issue is not resolved, call Technical Support.
Console does not shutdown	• Operating System issue or file corruption	1. Hold the Silver power button on the front down for approximately 10 seconds. The Console should shutdown. 2. If the above does not work, power the Console off with the switch on the back. 3. Contact Technical Support

		if the issue remains.
Audible alarm tone does not sound after boot-up process	• Speaker hardware failure	1. Contact Technical Support.
Failed Water Trap / Sample Line Leak Test	• Incorrectly connected the Sample Line to the CAL Port • Test timed out at 60 seconds • Sample line valve not closed properly • Loose gas lines connections • Water Trap not sealed completely • Water Trap seal leak	1. Ensure proper line connections. 2. Conduct test within 60 seconds. 3. Move the blue stopcock to the closed position. 4. Check Water Trap seal. 5. Replace Water Trap. 6. If issue is not resolved, call Technical Support
Cassette does not automatically eject from Console	• Mechanism malfunction	1. Open Cassette Access Door. Simultaneously push the tabs above and below the Cassette to manually eject the Cassette.
Screen Unresponsive	• Screen is frozen	1. Switch to Back-up Console. 2. Hold Silver Power Button for 10 seconds. 3. Wait for Console to shut down. 4. Switch off and on black rocker switch. 5. Reboot Console.
Adaptive Sensor Not Detected	• Adaptive Sensor Cable Not Connected • Adaptive Sensor not Connected to Adaptive Sensor Cable	1. Verify Adaptive Sensor Cable is properly plugged into front of Console and the cable is fully inserted. 2. Detach the Adaptive Sensor from the Adaptive Sensor Cable. 3. Wait at least five seconds. 4. Reattach the Adaptive Sensor to the Adaptive Sensor Cable.
	• Respiratory Device not delivering flow into circuit	1. Ensure Respiratory Device is delivering flow into circuit

Flow Not Detected	• Adaptive Sensor not present in circuit	circuit. 2. Verify Adaptive Sensor is connected in the circuit.
Adaptive Sensor Icon is Yellow	• Adaptive Sensor is not properly connected or has become disconnected • Adaptive Sensor is malfunctioning	1. Detach the Adaptive Sensor from the Adaptive Sensor Cable. 2. Unplug the Adaptive Sensor Cable from the Console. 3. Wait at least five seconds and reinsert the Adaptive Sensor Cable into the Console. 4. Reattach the Adaptive Sensor to the Adaptive Sensor Cable. 5. If problem persists, replace the Adaptive Sensor. 6. If problem still persists, call Technical Support.

SECTION 9
SYSTEM MAINTENANCE

9. SYSTEM MAINTENANCE

9.1 Calibration

This section describes the process for performing high and low calibration for NO, NO_2, and O_2. Calibration of the GENOSYL DS should be performed every 14 days to ensure the accuracy of NO, NO_2, and O_2 measurements. All calibrations can be performed at any time the Console is powered on, including while actively dosing. Air calibrates the low range for the NO and NO_2 sensors. The high range of the NO and NO_2 sensors are calibrated by using calibration gas tanks. The software will notify the user when calibration is due.

The display within the calibration tab provides the status and the calibration due date of the different types of sensors. Air calibration provides the time of the last calibration

since the System automatically performs this calibration every 4 hours while actively dosing or every 24 hours while powered on. A green check under status indicates that sensor has successfully been executed within the calibration period. A red X under status indicates that the sensor has not successfully been executed within the calibration period.

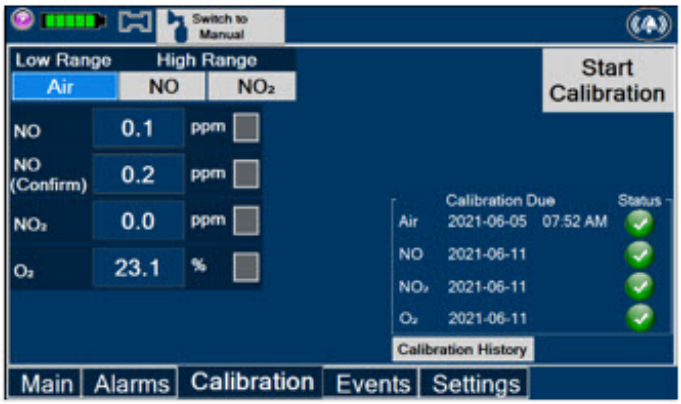
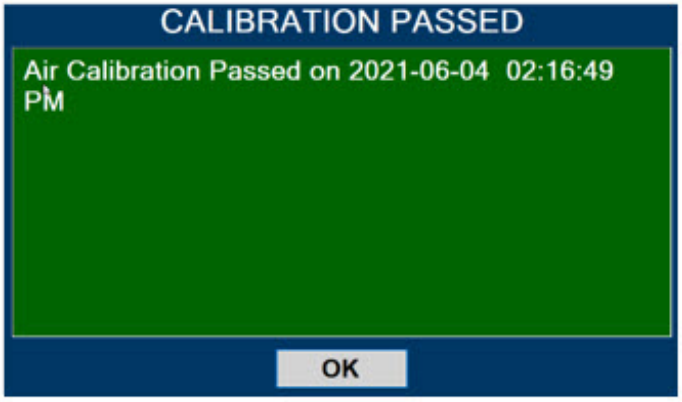
During calibration, the display will provide measured readings from each sensor. Note, there are two redundant NO sensors which are used to verify and ensure accuracy of the dosage provided by the System. During calibration, the display will provide a real-time status of the test with colored boxes to the right of the displayed sensor output. A yellow box indicates that the sensor is being calibrated. A green box indicates that calibration was successful for that sensor. A red box indicates that calibration for that sensor failed.

WARNING
• ONLY use the calibration gas pressure regulators supplied by the manufacturer. Pressure regulators not supplied by the manufacturer may damage the sensors and may lead to patient injury. • ALWAYS verify the correct NIST traceable calibration gas is being used and confirm the expiration date of the calibration gas prior to performing calibration. The use of incorrect or expired gas may result in inaccurate sensor readings and can lead to patient injury. • NEVER perform NO or NO_2 calibration within the MR scanner room. Calibration equipment is a potential projectile hazard.

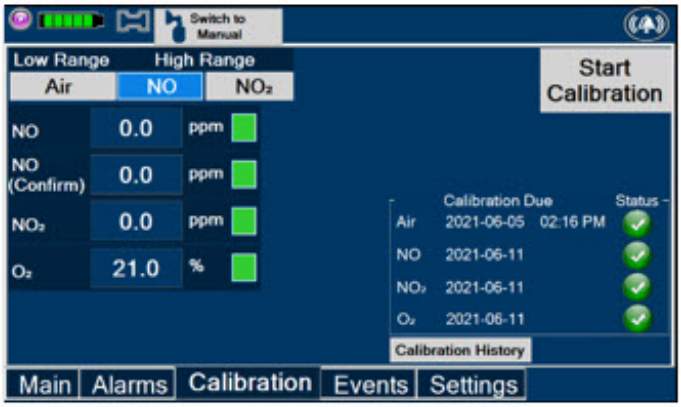
CAUTION
• ALWAYS perform a full-scale calibration of the GENOSYL DS when prompted by the System prior to use. • ALWAYS confirm the correct flow direction of the installed one-way check valve in the sampling tee to avoid over pressurization of the sample system and damage to the device.

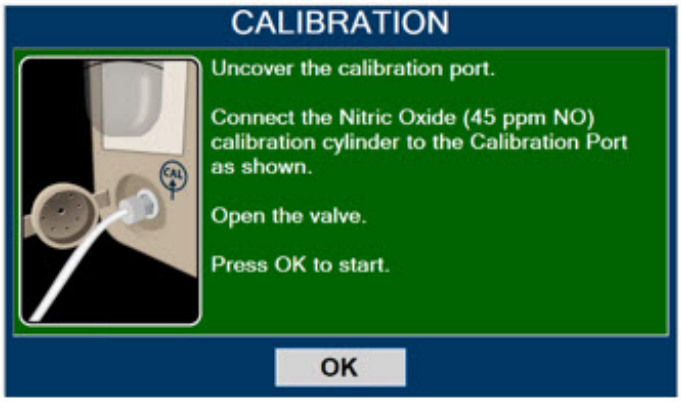
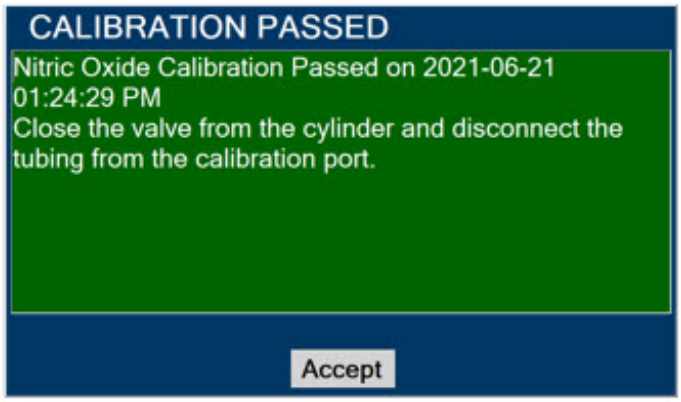
9.1.1 Air Calibration

DISPLAY	ACTION	Warnings, Cautions and Notes
	1. **Check** to make sure nothing is connected to the CAL port during	**NOTE** Air Calibration will take up to 2 minutes

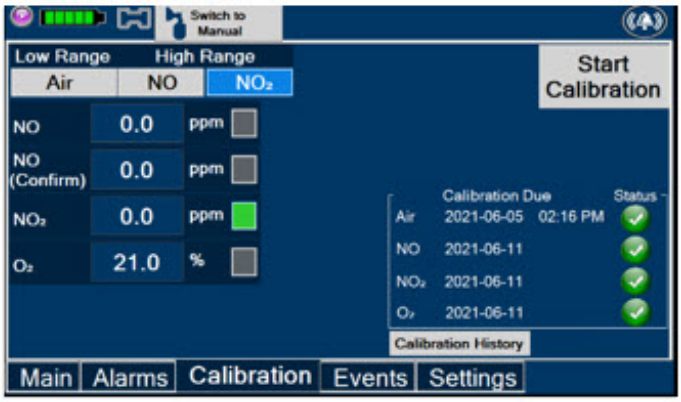
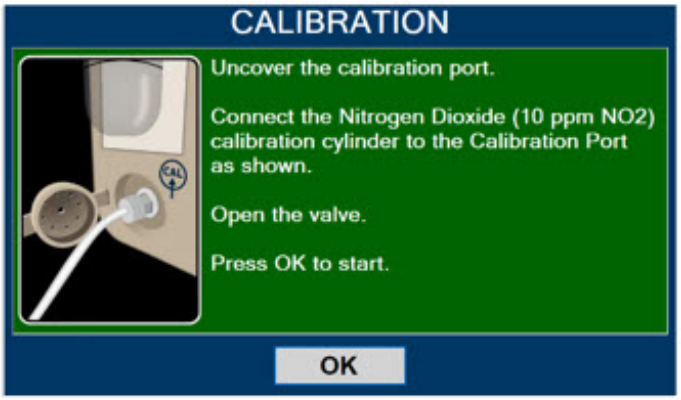
	Air Calibration. 2. If the Calibration Tab is not displayed, **press**the "Menu" tab to access the sub-level tabs. 3. **Press**the "Calibration" tab on the display menu. 4. **Press**the Low Range "Air" button. 5. **Press**the blue "Start Calibration" button.	if not dosing, or 5 minutes if actively dosing. A progress bar is displayed in the lower left-hand corner of the display screen during the calibration process.
	1. **Press**"OK" to continue once calibration is complete.	**NOTE** If air calibration fails, ensure that nothing is connected to or blocking the CAL port.

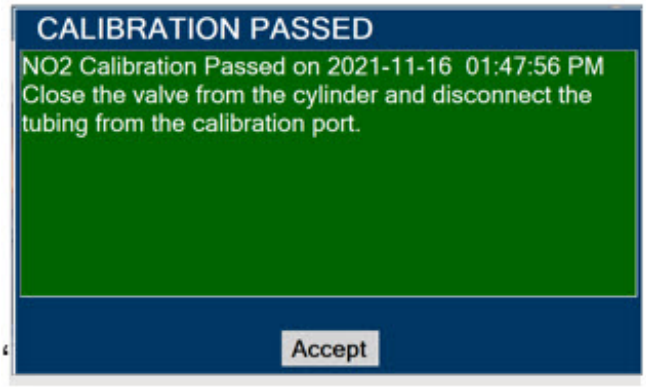
9.1.2 NO Calibration

DISPLAY	ACTION	Warnings, Cautions and Notes
	1. If the Calibration Tab is not displayed, **press**the "Menu" tab to access the sub-level tabs. 2. **Press**the "Calibration" tab on the display menu. 3. **Press**the High Range "NO" button. 4. **Press**the gray "Start Calibration" button.	
		WARNING DO NOT open the valve

	1. **Follow**the onscreen instructions.	prior to connecting to the CAL port. Opening the valve first will expose the user to NO gas. DO NOT interrupt calibration until finished. If interrupted, the calibration will be cancelled. **NOTE** NO calibration takes approximately 2 minutes if not dosing, or 5 minutes if actively dosing. A progress bar is displayed in the lower left-hand corner of the display screen during the calibration process.
	1. **Follow**the onscreen instructions 2. **Press**"Accept" to continue once calibration is complete.	**WARNING** DO NOT disconnect tubing from the calibration port prior to closing the valve. Disconnecting the tubing first will expose the user to NO gas.

9.1.3 NO $_2$Calibration

DISPLAY	ACTION	Warnings, Cautions and Notes
	1. If the Calibration Tab is not displayed, **press** the "Menu" tab to access the sub-level tabs. 2. **Press** the "Calibration" tab on the display menu. 3. **Press** the High Range "NO_2" button. 4. **Press** the gray "Start Calibration" button.	
	1. **Follow** the onscreen instructions.	**WARNING** DO NOT open the valve prior to connecting to the CAL port. Opening the valve first will expose the user to NO_2 gas. DO NOT interrupt calibration until finished. If interrupted, the calibration will be cancelled. **NOTE** NO_2 calibration takes approximately 2.5 minutes. A progress bar is displayed in the lower left-hand corner of the display screen during the calibration

		process.
	1. **Follow**the onscreen instructions. 2. **Press**"OK" once calibration is complete.	**WARNING** DO NOT disconnect tubing from the calibration port prior to closing the valve. Disconnecting the tubing first will expose the user to NO_2 gas.

9.2 Maintenance Schedule

The Console components require the following maintenance:

COMPONENT	SCHEDULE
Water Trap	Per patient or as required (per Water Trap/ Sample Line Leak Test)
GaussAlert™	Monthly functionality check
Console	Yearly

The Console requires yearly factory service. The System will display an Information Message to remind the operator when service is required. Call **Technical Support at 877-337-4118**for support or to schedule service.

9.3 Testing the GaussAlert™ Function

WARNING

- Keep the test magnet tool away from pacemakers, ICDs, and other implanted medical devices.
- If either GaussAlert™ fails testing (does not alarm when the magnet tool is used), contact **Technical Support at 877-337-4118**to request a replacement.
- Do not use the GENOSYL DS in the MR Environment if neither GaussAlert™ is functional.

CAUTION

- Do not use or store the test magnet tool in the MR scanner room.
- Keep the test magnet tool away from the GENOSYL DS user screen. Neodymium magnets can damage computer monitors, watches, pulse oximeters, and other mobile handheld devices.
- Keep the test magnet tool away from magnetic media such as credit cards, magnetic I.D. cards, cassette tapes, video tapes, or other such devices.

NOTE
If the LED stay illuminated for longer than a brief flash, or does not illuminate at all, the battery needs to be replaced. Contact **Technical Support at 877-337-4118**to request a replacement.

To use the GaussAlert™ test magnet tool to test alarm function, follow the steps listed below.

1. Place the test magnet tool on the GaussAlert™ alarm bracket in the area identified in Figure 23.
2. The alarm will activate and a short flash (less than two seconds) of the LED indicates proper function.
3. Move the test magnet tool away from the GaussAlert™ until the alarm stops sounding.
4. Repeat this procedure on the second GaussAlert™.

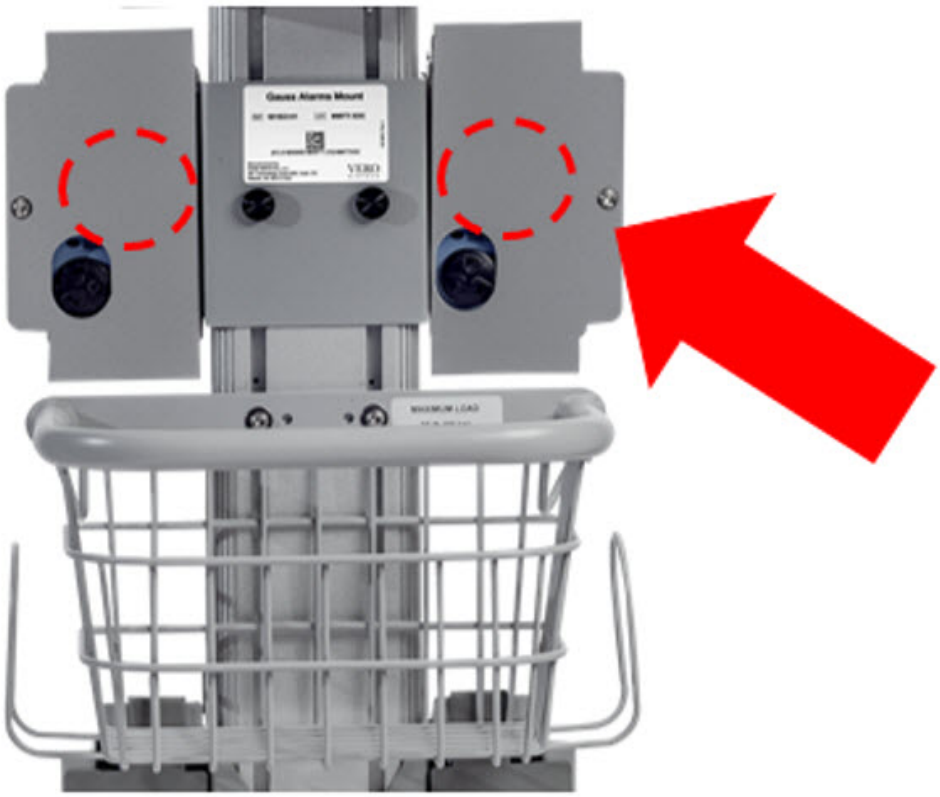


Figure 23: GaussAlert™ Test

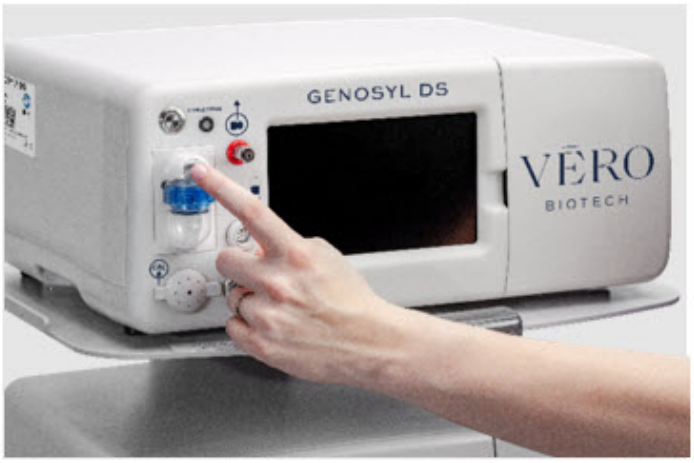
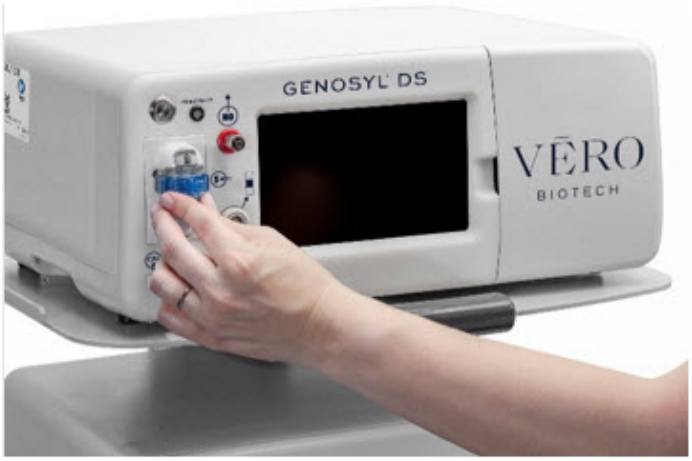
9.4 Water Trap Maintenance

The following section will describe the emptying of the Water Trap. The Water Trap should be emptied when the liquid contents reach the horizontal black line marked on the Water Trap.

Prior to emptying the Water Trap, ensure the Gas Sample Line is removed and reattached after emptying the Water Trap.

9.4.1 Emptying the Water Trap

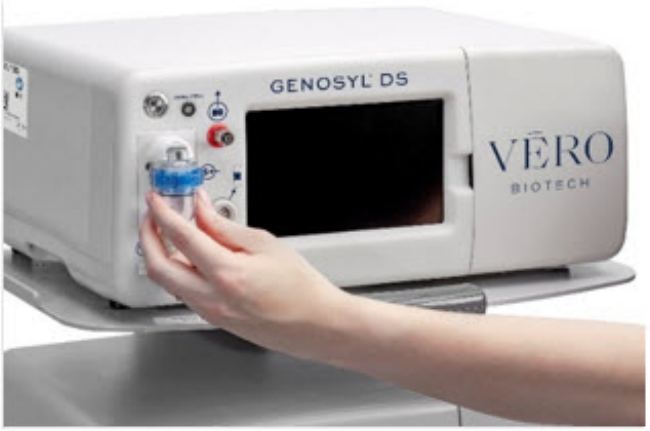
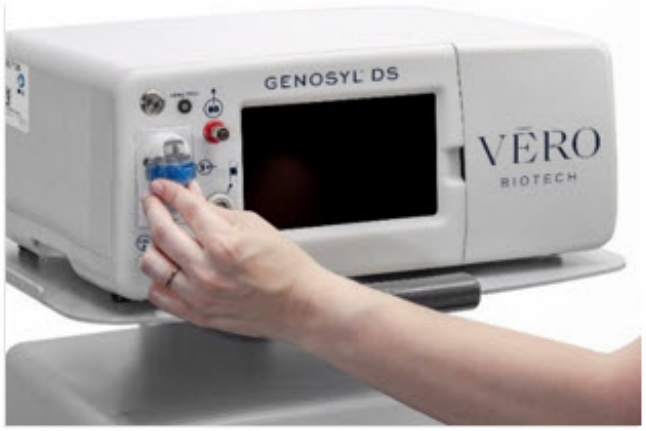
WARNING
ALWAYS empty Water Trap before each use, when prompted by the System, and when the trap is more than half full. Allowing the Water Trap to completely fill will occlude the Sample Line which will interrupt patient gas NO, NO_2, and O_2 concentration monitoring. Failure to monitor the patient gas NO, NO_2, and O_2 concentrations may result in patient injury.

DISPLAY	ACTION
	1. **Remove** Water Trap from Console by lifting latch and pulling the base of the Water Trap away from the Console. 2. **Remove** the lid by pulling the lid from the base. 3. **Empty** the liquid contents.
	1. **Reattach** the lid by pushing it back onto base. 2. **Slide** the Water Trap back on the Console until it clicks into place.

9.4.2 Water Trap Replacement

If the Water Trap / Sample Line Leak Test fails, and Sample Gas Line integrity is confirmed with blue stopcock in place, replace the Water Trap.

WARNING
• ALWAYS use a Water Trap supplied by the manufacturer. Using an incorrect water trap could result in non-functioning or inaccurate sensor readings. • ALWAYS conduct Water Trap/ Sample Line Leak Test every time you empty or replace the Water Trap, as failure to do so may lead to an incorrect NO reading, which can result in injury or death.

DISPLAY	ACTION
	1. **Remove**old Water Trap from Console by lifting the latch and pulling the base of the Water Trap away from the Console.
	1. **Slide**new Water Trap back on the Console until it clicks into place. Replace sample line to Water Trap. 2. **Discard**the old Water Trap.

9.5 Battery

The battery will be serviced during scheduled maintenance performed by the manufacturer. If the need arises to replace the battery sooner than scheduled contact **Technical Support at 877-337-4118**to schedule a maintenance appointment.

During storage, the GENOSYL DS may be stored with the power off, but the external power supply should be connected at least once every 3 months to ensure a minimum charge is maintained on the internal battery (see Section 11.1.5for additional information).

WARNING
ONLY properly trained personnel should replace the battery. Incorrectly replacing the battery may result in a hazard such as excessive temperatures, fire, or explosion.

9.6 Cleaning

9.6.1 Enclosure, Connections, and Surfaces Other Than the Display

Prior to performing any cleaning or maintenance operations ensure that the GENOSYL DS Console has been completely powered down as specified in Section 6.1 and that the AC/DC power supply external to the GENOSYL DS Console has been unplugged. Apply any mild detergent to cloth prior to wiping the System. Gently clean the outer surface of the Console, Cart, and Adaptive Sensor Cable with a soft damp cloth and mild detergent or isopropyl alcohol (70%).

CAUTION
• DO NOT sterilize (e.g., autoclave, gas sterilize) any of the components of the System, as this may compromise performance. • DO NOT use harsh cleaning agents (see Table 6) on the GENOSYL DS. Doing so may impair the structural integrity and/or function of the device. • ONLY use a damp cloth to clean the Console and limit use of liquids around Console. Excess water can permanently damage the device. • ALWAYS ensure the System is completely dry after cleaning before powering it ON. Failure to do so could result in equipment damage.

WARNING
• NEVER submerge the GENOSYL DS, Cassette, or non-disposable Adaptive Sensor Cable. Submerging in liquid will damage the System and could cause electrical shorts which may result in injury or death. • DO NOT clean the GENOSYL DS with the power connected and the System turned ON, as this may lead to injury (e.g., shock). Unplug AC/DC power supply external to the System prior to cleaning.

Table 6: Recommended Cleaning Agents

CLEANING AGENT	ACTIVE INGREDIENTS
Avert by Diversey	Sodium hypochlorite 1.312% Other ingredients 98.688%
Oxivir by Diversey	Hydrogen Peroxide 0.5% Other ingredients 99.5%
CaviWipesXL by Metrex	Disobutylphenoxyethxyethyl dimethyl benzyl ammonium chloride 0.28% Isopropanol 17.20% Inert ingredients 82.52%
Sani-Cloth AF3 by PDI Healthcare	n -Alkyl dimethyl ethybenzyl ammonium chlorides 0.14% n-Alkyl dimethyl benzyl ammonium chlorides 0.14% Other ingredients 99.72%
Super Sani-cloth by PDI Healthcare	n -Alkyl dimethyl ethybenzyl ammonium chlorides 0.25% n-Alkyl dimethyl benzyl ammonium chlorides 0.25% Isopropyl Alcohol 55.00% Other ingredients 44.50%

9.6.2 Display Screen

Turn off Console and disconnect from AC power. Gently clean with a damp cloth.

CAUTION
• DO NOT touch or rub the display screen with abrasive cleaning compounds or organic solvents, as they may scratch and damage the screen.

- DO NOT spray or pour liquids directly on the controller or the display, as they may damage the screen.

9.6.3 Cleaning the Gauss Alarms Mount

Use a soft cloth dampened with water to clean the enclosure. Use an aqueous solution of up to 75% isopropyl alcohol for more efficient cleaning. Disinfection may be accomplished with the use of denatured alcohol.

9.7 Storage

9.7.1 Cart / Console Storage

The acceptable storage conditions for the Cart/Console are shown in the following table.

Cart / Console Storage	Temperature	-20^0 C to 60^0 C
	Humidity	15% to 95%, non-condensing
	Pressure	57 kPa to 110 kPa

During storage, the GENOSYL DS may be stored with the power off, but the external power supply should be connected at least once every 3 months to ensure a minimum charge is maintained on the internal battery (see Section 11.1.5for additional information).

WARNING
• MAKE SURE the GENOSYL DS is connected to AC wall power to charge the battery a minimum of once every 3 months to maintain a minimum battery charge. Failure to recharge the Console battery for extended timeframes may result in full discharge of the battery. If a Battery Error message occurs during startup of the System, contact **Technical Support at 877-337-4118**for assistance. • ONLY properly trained personnel should replace the battery. Incorrectly replacing the battery may result in a hazard such as excessive temperatures, fire, or explosion. • ONLY store the GENOSYL DS as outlined in the storage instructions. Not storing the device in alignment with its storage instructions can cause the device to be unsafe and lead to injury or death.

9.7.2 Cassette / Accessory Storage

GENOSYL DS may not function correctly if the Cassette or any of the System Accessories have been exposed to high levels of heat or humidity. Cassettes are supplied in a plastic container and should remain unopened until use. Cassettes should be stored at 25°C (77°F) with excursions permitted between 15°C to 30°C (59°F to 86°F). (See USP Controlled Room Temperature).

SECTION 10
MECHANICAL VENTILATION

10. MECHANICAL VENTILATION

WARNING
• ONLY mechanical ventilators validated with the GENOSYL DS should be used. Not using a validated ventilator system can result in injury or harm. • DO NOT use the GENOSYL DS with circle anesthesia ventilator systems. The GENOSYL DS has not been characterized or qualified for use with anesthesia breathing systems with recirculation of gases.

10.1 Mechanical Ventilation

There are two main effects of connecting the GENOSYL DS to a ventilator breathing circuit:

- The System injects up to 0.9 LPM of NO/air (21% Oxygen) into the inspiratory output of the ventilator.
- The System samples up to 0.3LPM from the ventilator circuit as a measurement to the built-in gas analyzers

The results of adding and subtracting gas into the ventilator circuit are described in sections 10.1.1 to 10.1.4:

10.1.1 Oxygen Dilution

The ventilator typically is flowing gas to the patient with enhanced oxygen content from room air at 21% to pure oxygen at 100%. The DS is injecting the NO in air with a concentration of oxygen at nominally 21%. Thus, except for the case where the ventilator is supplying gas to the patient at 21% oxygen, there is some dilution of the oxygen to the patient. This dilution is given by the following equation:

$$\text{Percent } O_2 \text{ to Patient} = [\{\%O_2/100 + (\text{Flow}_{inj}/\text{Flow}_{vent}) \times 0.21\}/\{1 + (\text{Flow}_{inj}/\text{Flow}_{vent})\}] \times 100$$

Where:

1. Flow_{inj} = Injection flow in same units as ventilator flow
2. Flow_{vent} = Ventilator flow in same units as injection flow
3. $\%O_2$ = Percent oxygen out of ventilator
4. 0.21 = Fraction of oxygen in injection flow (21%)

The table below shows the effect on the actual concentration of oxygen supplied to the patient for set ventilator flow settings with a nominal flow of 0.6 LPM of NO/air (21% Oxygen) into the inspiratory output of the ventilator.

Table 7: Oxygen Dilution

	Oxygen (%) Supplied from Ventilator				
	100	**80**	**60**	**40**	**21**
Ventilator Flow (LPM)	**Oxygen (%) Delivered to Patient**				
20	98	78	59	39	21
15	97	78	59	39	21
10	96	77	58	39	21
9	95	76	58	39	21
8	94	76	57	39	21
7	94	75	57	39	21
6	93	75	56	38	21
5	92	74	56	38	21
4	90	72	55	38	21
3	87	70	54	37	21

10.1.2 Minute Volume

When using volume ventilation with the GENOSYL DS, the tidal volume delivered to the patient may show small changes due to the addition and subtraction of gases by the Delivery System. Some minor ventilator adjustments to the minute volume may be required. Maximum total flow added to the ventilator circuit is 0.9 LPM of concentrated NO gas and the maximum total flow removed from the ventilator circuit is 0.3 LPM of sampled gas.

10.1.3 Trigger Sensitivity

The addition and subtraction of gases by the GENOSYL DS 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 less than the total flow added to the System.

10.1.4 Maximum NO Delivery

The maximum combination of dose (ppm) and flow (LPM) is 800. ppm x LPM (e.g., 20 ppm with 40 LPM, 40 ppm at 20 LPM, etc.). The System is capable of delivering NO at a minimum of 1 ppm x LPM (e.g., 1 ppm at 1 LPM). See the graph below for the minimum and maximum dose ranges for the System, based on ventilator circuit total minute volume.

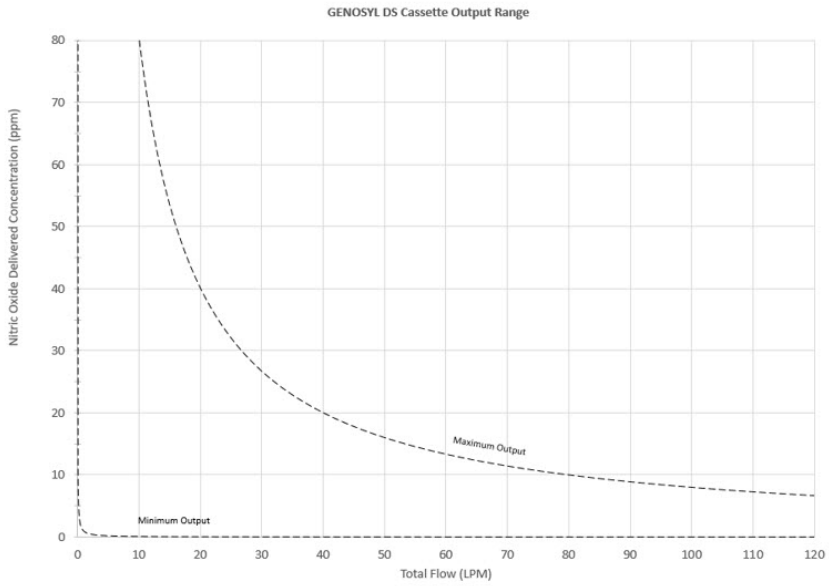


Figure 24: Cassette Output Range

10.2 Ventilator Compatibility

The GENOSYL DS is compatible with the following equipment and accessories.

Table 8: Compatible Equipment and Accessories

MANUFACTURER	TYPE OF EQUIPMENT	MODEL
Fisher Paykel	Vent circuit kit	RT265
Fisher Paykel	Vent circuit kit	RT210
Fisher Paykel	Humidifier	850
Fisher Paykel	Humidifier Chamber	MR 290
		Resus Hyperinf System 1/2L

Medline	Hyperinflated Resuscitator	Resus Hyperinf System 1/2L-LF
Laerdal	Self-inflated Resuscitator	Infant Silicone Resuscitators

VERO Biotech performs validation testing which determines the compatibility of ventilator/gas delivery systems with the GENOSYL DS. During this compatibility testing, the GENOSYL DS is evaluated for the following parameters while connected to each ventilator/gas delivery system:

- **NO Dose Accuracy:**Continuous and accurate delivery of a targeted dose of Nitric Oxide within ± 20% of setpoint or within +/- 2 ppm, whichever is greater.
- **Respiratory Device Breath Delivery and Alarms:**The respiratory device breath delivery and alarms continue to function as intended by the manufacturer across the range of operating conditions.
- **NO $_2$Performance:** NO $_2$remains within acceptable limits less than 1.0 ppm with 60% FiO $_2$and ≤40 ppm NO.
- **O $_2$Dilution:** Post dilution O $_2$level delivery is maintained within acceptable limits and conforms with the information presented in the GENOSYL DS Operator's Manual, Section 10.1.1, "Oxygen Dilution".
- **NO Concentration Transients:**NO concentration transients are ≤150% of mean concentration and as low as 0.0 ppm as long as the transient duration does not exceed 10% of the volumetric duration of the breath.

The testing performed demonstrated conformance with all specified requirements. The following ventilators and non-invasive gas delivery systems in Table 9 have been validated for use with the GENOSYL DS. See Section 3.2for use configurations.

Use of a Mixer is recommended when delivering in specific tidal volume ranges on various ventilation devices. Refer to Table 10 for when a Mixer is and is not recommended.

WARNING
• ALWAYS use the GENOSYL DS in accordance with the indications, usage, contraindications, warnings, and precautions described in the GENOSYL prescribing information and labeling. Refer to latest approved prescribing information and labeling prior to use. • The approved patient population for the GENOSYL DS as specified in the drug labeling for GENOSYL (nitric oxide) for inhalation, is limited to neonates. The GENOSYL DS is not intended to be used in other patient populations.

Table 9: Details of Validated Systems

Manufacturer	Model	Neonatal	Pediatric/Adult	CPAP	HFNC	MR
Bio-Med Devices	Crossvent 2+/2i+	•	•			
Bio-Med Devices	MVP-10	•	•			
Dräger	VN500	•	•			
Dräger	V500	•	•			
GE Healthcare	R860	•	•			
Hamilton	C1/T1	•	•			

Hamilton	C2/C3	•	•			
Hamilton	MR1	•	•			•
Hamilton	G5	•	•			
Maquet	Servo-U/N/I	•	•			
Maquet	Servo-I MR	•	•			•
Puritan Bennett	840	•	•			
Puritan Bennett	980	•	•			
Vyaire Medical Inc.	AVEA	•	•			
Fisher & Paykel	Optiflow Junior Breathing Circuit				•	
Fisher and Paykel	Optiflow Breathing Circuit			•		
Fisher & Paykel	Bubble CPAP System			•		

See Section 3.4for assembly instructions for Injection Assembly with Adaptive Sensor and Mixer Assembly with Adaptive Sensor.

Table 10: Validated Compatibility with and without Inline Mixer

Manufacturer	**Model**	**Ventilator Range Tested: Neonatal**	**Ventilator Range Tested:**	
			Pediatric/Adult	
		Ventilator Circuit using Injection Assembly with Adaptive Sensor	**Ventilator Circuit using Injection Assembly with Adaptive Sensor**	**Ventilator Circuit using Mixer Assembly with Adaptive Sensor**
		(Without Inline Mixer)	**(Without Inline Mixer)**	**(With Inline Mixer)**
Bio-Med Devices	Crossvent 2+/2i+	•	•	N/A
Bio-Med Devices	MVP-10	•	•	N/A
Dräger	VN500	•	•	N/A
Dräger	V500	•	VT < 400 mL	VT > 400 – 600 mL
GE Healthcare	R860	•	VT < 350 mL	VT > 350 – 650 mL
Hamilton	C1/T1	•	VT ≤ 450 mL	VT > 450 – 600 mL
Hamilton	C2/C3	•	VT ≤ 470 mL	VT > 470 – 950 mL
Hamilton	MR1	•	VT ≤ 470 mL	VT > 470 – 950 mL
Hamilton	G5	•	VT ≤ 950 mL	VT > 950 – 1400 mL
Maquet	Servo-U/N/I	•	VT ≤ 650 mL	VT > 650 – 740 mL
Maquet	Servo-I MR	•	VT ≤ 650 mL	VT > 650 – 740 mL
Puritan Bennett	840	•	VT ≤ 300 mL	VT > 300-760 mL
Puritan Bennett	980	•	VT ≤ 485 mL	VT > 485 – 1100 mL
Vyaire Medical Inc.	AVEA	•	VT < 540 mL	VT ≥ 540 mL

Key:

• : Range Fully tested; use of Inline Mixer is not required
VT: Tidal Volume
VT Value listed: Tidal volumes in this range have been validated in accordance with column header (with or without Inline Mixer)

GENOSYL ®DS

SECTION 11
PRODUCT SPECIFICATIONS

11 PRODUCT SPECIFICATIONS

11.1 System Performance

NO DOSING	
Accuracy	+/- 20% or +/- 2 ppm (whichever is greater)
Range	0 to 80 ppm
Flow rate (max)	900 mL/min

GAS SENSOR			
	Range	**Resolution**	**Accuracy**
NO	0 - 10 ppm	0.1 ppm	≤20 ppm: +/- (20% of actual concentration + 0.5) >20 ppm:+/- (10% of actual concentration + 0.5)
	10 – 100 ppm	1 ppm	
NO_2	0.0 - 12 ppm	0.1 ppm	+/- (20% of actual concentration + 0.5 ppm)
O_2	18 - 100%	1%	+/- volume fraction of 2.5% +2.5% of gas level

11.1.1System Classification

- Class I equipment
- Ordinary Equipment IPX1
- Continuous Use
- Essential Performance: The System shall continue to deliver a controlled dose, as configured by the user (e.g., 20 ppm @ 6 LPM within +/- 20%) with NO_2< 3 ppm and O_2= 21 +/- 3% in room air for the specified range of use conditions.

11.1.2 Testing

- ANSI ES 60601-1
- IEC 60601-1-2
- IEC 60601-1-8

11.1.3 Electrical

NOTE
Disconnect main power cord from the wall outlet to isolate equipment from main power. Do not position equipment to make it difficult to disconnect equipment from main power.

11.1.4 Power Supply

- Medical Grade Class I
- Input: 100-240 V, 50-60 Hz, 2A
- Output: 18 V DC, 8.3 A
- 150 Watts Max

11.1.5 Battery

- Fully charged Back-up battery that provides at least 1 hour of uninterrupted Nitric Oxide delivery in the absence of an external power source.
- Typical battery life is 300 charge/discharge cycles.
- The battery will be serviced during scheduled maintenance performed by the manufacturer.
- If the need arises to replace or dispose of the battery sooner than scheduled contact

Technical Support to schedule a maintenance appointment.

The battery has an embedded 5 segment LCD battery indicator viewable through side panel window. The segments will display the following information:

- 5 segments filled – 81%-100% charged
- 4 segments filled – 61%-80% charged
- 3 segments filled – 41%-60% charged
- 2 segments filled – 21%-50% charged
- 1 segment filled – 1% - 20% charged
- No battery indication – below 1%
- Most significant segment flashing – charging
- Most significant segment not flashing – not charging

11.1.6 Display

- Touch screen – Resistive
- Brightness – 400 cd/m ^{2}
- Resolution – 800 × 480 pixels, color

11.2 Mechanical

CART	
Weight	18.15 kg (40.01lbs)
Width × Length	47.8 cm (18.8 in) × 66.7 cm (26.3 in)
Height	120.7 cm (47.5 in)

CONSOLE	
Weight	8.85 kg (19.75 lb)
Width × Length	40.6 cm × 30.5 cm (16 in × 12 in)
Height	17 cm (6.75 in)

CASSETTE	
Weight	0.42 kg (0.93 lb)
Width × Length	11.4 × 3.8 cm (4.5 in × 1.5 in)
Height	13 cm (5.1in)

11.3 Environmental

ENVIRONMENTAL RANGES		
Operating	Temperature	5^o C to 40^o C
	Humidity	15% to 95%, non-condensing
	Pressure	57 kPa to 110 kPa
	Altitude	Under 15,000 feet
Storage	Temperature	-20^o C to 60^o C
	Humidity	15% to 95%, non-condensing
	Pressure	57 kPa to 110 kPa

	Altitude	Under 15,000 feet
Water Ingress Protection	IPX1	

11.4 GaussAlert™ Specifications

Standard Factory Preset Alarm Thresholds	100 Gauss (10 mT)
Audio Alarm Typical Sound Pressure	92dB (A) at 24 inches
Audio Alarm Frequency	2900 Hz +/- 250Hz
Typical Battery Life	5 years
Sensor Type	Mechanical with panoramic uniform sensitivity

11.5 MR Signal-to-Noise Ratio and Artifact Dimension Analysis

MR image artifact was evaluated using 1.5 T and 3 T MRI Systems. Testing was conducted using standard American College of Radiology (ACR) sequences and a standard ACR large phantom placed inside a transmit-receive head coil. Duplicate sequences were performed to acquire the same images with and without the GENOSYL DS Nitric Oxide Delivery System operating on battery power inside the MRI suite.

The GENOSYL DS compatibility test results are as follows:

Artifact Dimensional Analysis	1.5 T	The maximum dimensional change in images acquired during the operation of the GENOSYL DS was < 1 mm.
	3 T	The maximum dimensional change in images acquired during the operation of the GENOSYL DS was < 1 mm.
Image Quality Signal-to-Noise Ratio Analysis	1.5 T	The average SNR change was -35%. The average SFNR change was -42%. The PIU values were all 96%.
	3 T	The average SNR change was -25%. The average SFNR change was -22%. The PIU values were all greater than 94%.

The GENOSYL DS does not distort the geometric accuracy and the image intensity uniformity is not adversely affected by the presence of the GENOSYL DS at the 100 Gauss line. The SNR and SFNR are both impacted by the presence of the GENOSYL DS, to a more pronounced degree when the equipment is powered via a wall outlet inside the MRI suite versus operating on the battery.

NOTE

- The test results presented here were obtained with the GENOSYL DS operating on battery power.
- If using the GENOSYL DS while connected to wall power, it is recommended to route the power cords through a waveguide.

11.6 EMI/EMC

Emissions test	Compliance	Electromagnetic Environment – Guidance
RF emissions CISPR 11	Group 1 Class B	The GENOSYL DS uses RF energy only for its internal function. Therefore, its RF emissions are very low and are not likely to cause any interference in nearby electronic equipment. The GENOSYL DS is suitable for use in all establishments, including domestic establishments and those directly connected to the public low voltage power supply network that supplies buildings used for domestic purposes.
RF conducted emissions per CISPR 11 Ed. 5.1b:2010	Class B	The GENOSYL DS is suitable for use in all establishments, including domestic establishments and those directly connected to the public low voltage power supply network that supplies buildings used for domestic purposes.
Harmonic emissions IEC 61000-3-2	Class A	
Voltage fluctuations/flicker emissions IEC 61000-3-3	Complies	

Guidance and Manufacturer's Declaration – Electromagnetic Immunity			
The GENOSYL DS is intended for use in the electromagnetic environment specified below. The customer or the user of the GENOSYL DS should assure that it is used in such an environment			
Immunity Test	**IEC 60601 Test Level**	**Compliance Level**	**Electromagnetic Environment - Guidance**
Electrostatic discharge (ESD) IEC 61000-4-2	±8 kV contact ±15 kV air	±8 kV contact ±15 kV air	The relative humidity should be at least 5%.
Electrical fast transient/burst IEC 61000-4-4	±2 kV for power supply lines	±2 kV for power supply lines	Mains power quality should be that of a typical commercial or hospital environment.
Surge IEC 61000-4-5	AC line: Line to Line ±0.5kV, ±1 kV & Line to GND ±0.5kV, ±1 kV, ±2kV	AC line: Line to Line ±0.5kV, ±1 kV & Line to GND ±0.5kV, ±1 kV, ±2kV	Mains power quality should be that of a typical commercial or hospital environment.
			Mains power should be that of a typical

Voltage dips, short interruptions and voltage variations on power supply input lines IEC 61000-4-11	0% during 0.5 cycle 0% (100% reduction) for 1 cycles 70% (30% reduction) for 25 cycles 0% for 250 cycles- Short interruptions	0% during 0.5 cycle 0% (100% reduction) for 1 cycles 70% (30% reduction) for 25 cycles 0% for 250 cycles- Short interruptions	commercial or hospital environment. If the user of the GENOSYL DS requires continued operation during power mains interruptions, it is recommended that the GENOSYL DS be powered from an uninterruptible power supply or a battery.
Power frequency (50/60 Hz) Magnetic field IEC 61000-4-8	30 A/m	30 A/m with dwell time of 60sec	Power frequency magnetic fields should be at levels characteristic of a typical location in a typical commercial or hospital environment.
NOTE: U ┬is the AC main voltage prior to application of the test level.			
Conducted RF IEC 61000-4-6	6 V rms 150 kHz to 80 MHz in ISM bands *	10 V 80% AM @ 1 kHz 150 kHz - 80 MHz in ISM bands,	Except as indicated on page 10-137, portable and mobile RF communications equipment, including cables, should be used no closer to any part of the GENOSYL DS than the recommended separation distance calculated from the equation applicable to the frequency of the transmitter. Recommended separation distance: d=1.2√P d=1.2√P d=1.2√P 80 MHz to 800 MHz d=2.3√P 800 MHz to 2.7 GHz where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter
Radiated RF IEC 61000-4-3	10 V /m 80MHz to 2.7 GHz	10 V /m 80 MHz to 2.7 GHz	

			manufacturer and d is the recommended separation distance in meters (m). † Field strengths from fixed RF transmitters, as determined by an electromagnetic site survey, ‡should be less than the compliance level in each frequency range. §Interference may occur in the vicinity of equipment marked with the following symbol: 

* The ISM (industrial, scientific and medical) bands between 150 kHz and 80 MHz are 6.765 MHz to 6.795 MHz; 13.553 MHz to 13.567 MHz; 26.957 MHz to 27.283 MHz; and 40.66 MHz to 40.70 MHz.

† The compliance levels in the ISM frequency bands between 150 kHz and 80 MHz and in the frequency range 80 MHz to 2.7 GHz are intended to decrease the likelihood that a portable communications device could cause interference if it is inadvertently brought into patient areas. For this reason, an additional factor of 10/3 is used in calculating the recommended separation distance for transmitters in these frequency ranges.

‡ Field strengths from fixed transmitters, such as base stations for radio (cellular cordless) telephones and land mobile radios, amateur radio, AM and F M radio broadcast and TV broadcast cannot be predicted theoretically with accuracy. To assess the electromagnetic environment due to fixed R transmitters, an electromagnetic site survey should be considered. If the measured field strength in the location in which the GENOSYL DS is used exceeds the applicable RF compliance level above, the GENOSYL DS should be observed to verify normal operation. If abnormal performance is observed, additional measures may be necessary, such as reorienting or relocating the GENOSYL DS.

§ Over the frequency range 150 kHz to 80MHz, field strengths should be less than 3 V/m.

NOTE
NOTE 1: At 80 MHz and 800 MHz, the higher frequency range applies. **NOTE 2**: These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.

Recommended separation distances between portable and mobile RF communications equipment and the GENOSYL DS
The GENOSYL DS is intended for use in an electromagnetic environment in which radiated RF disturbances are controlled. The customer or the user of the GENOSYL DS can help prevent electromagnetic interference by maintaining a minimum distance between portable and mobile RF communications equipment (transmitters) and the GENOSYL DS as recommended below, according to the maximum output power of the communications equipment except as indicated on page 10-166.

Rated Maximum Output Power of Transmitter W	Separation Distance According to Frequency of Transmitter, m		
	150 kHz to 80 MHz d=1.2√P	80 MHz to 800 MHz d=1.2√P	800 MHz 2.5 GHz d=2.3√P
0.01	0.12	0.12	0.23
0.1	0.38	0.38	0.73
1	1.2	1.2	2.3
10	3.8	3.8	7.3
100	12	12	23
For transmitters rated at a maximum output not listed above, the recommended separation distance d in meters (m) can be estimated using the equation applicable to the frequency of the transmitter, where P is the maximum output power rating of the transmitter in Watts (W) according to the transmitter manufacturer.			

Immunity Test	Standards Tested	Compliance Level	Electromagnetic Environment - Guidance
Radiated RF AIM 7351731 - Medical Electrical Equipment and System Electromagnetic Immunity Test for Exposure to Radio Frequency Identification Readers	• ISO 14223 (Annex A) • ISO/IEC 14443-3 (Type A) (Annex B) • ISO/IEC 14443-4 (Type B) (Annex C) • ISO/IEC 15693 (ISO/IEC 18000-3 Mode 1) (Annex D) • ISO/IEC 18000-7 (Annex E) • ISO/IEC 18000-63 Type C (Annex F) • ISO/IEC 18000-3 (Mode 3) • ISO/IEC 18000-4 Mode 1 (Annex G)	Per the Annex in the standard	System tested as compatible with RFID tags/communication

Frequencies of portable and mobile transmitters for which the recommended separation distance is 30 cm (12 in).

Band (MHz)	Service
380 - 390	TETRA 400
430 - 470	GMRS 460, FRS 460
704 - 787	LTE Band 13, 17
800 - 960	GSM 800/900 TETRA 800, iDEN 820, CDMA 850, LTE Band 5
1,700 – 1,990	GSM 1800; CDMA 1900; GSM 1900; DECT; LTE Band 1, 3, 4, 25; UMTS

2,400 – 2,570	Bluetooth, WLAN, 802.11 b/g/n, RFID 2450, LTE Band 7
5,100 – 5,800	WLAN 802.11 a/n

GENOSYL ®DS

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KEY WORD INDEX

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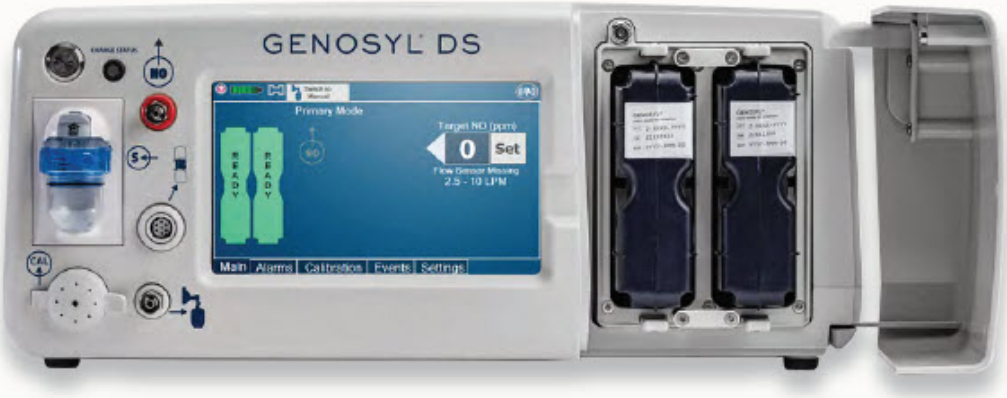
1 NIOSH Pocket Guide to Chemical Hazards, Dept of Health & Human Services, Centers for Disease Control and Prevention, National Inst for Occupational Safety & Health. Publication 2005-149, Sept 2007.
2 Hess et al, Use of Inhaled Nitric Oxide in patients with Acute Respiratory Distress Syndrome. Respiratory Care 1996; 41(5):424-446.
3 Phillips M, Hall TA, Sekar K, Tomey JL. Assessment of Medical Personnel Exposure to Nitrogen Oxides During Inhaled Nitric Oxide Treatment of neonatal and Pediatric Patients. Pediatrics. 1999;104(5):1095-1110.
4 Qureshi MA, Shah NJ, Hemmen CW, Thill MC, Kruse JA.Exposure of Intensive Care Nurses to Nitric Oxide and Nitrogen Dioxide during Therapeutic use of Inhaled Nitric Oxide in Adults with Acute Respiratory Distress Syndrome. Am. J. Crit Care, 2003;12(2):147-153.

VĒRO

BIOTECH

GENOSYL®

DELIVERY SYSTEM



FOR DELIVERY OF

GENOSYL®

(NITRIC OXIDE)
GAS FOR INHALATION

QUICK REFERENCE GUIDE

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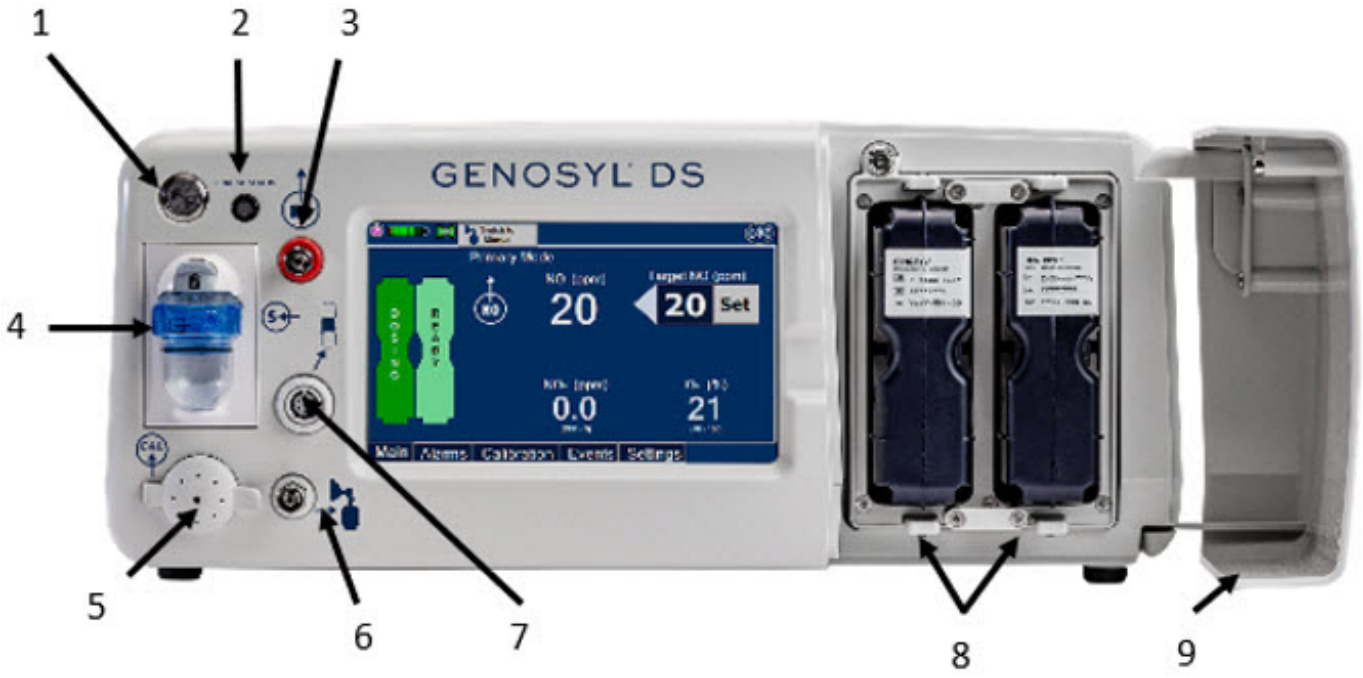
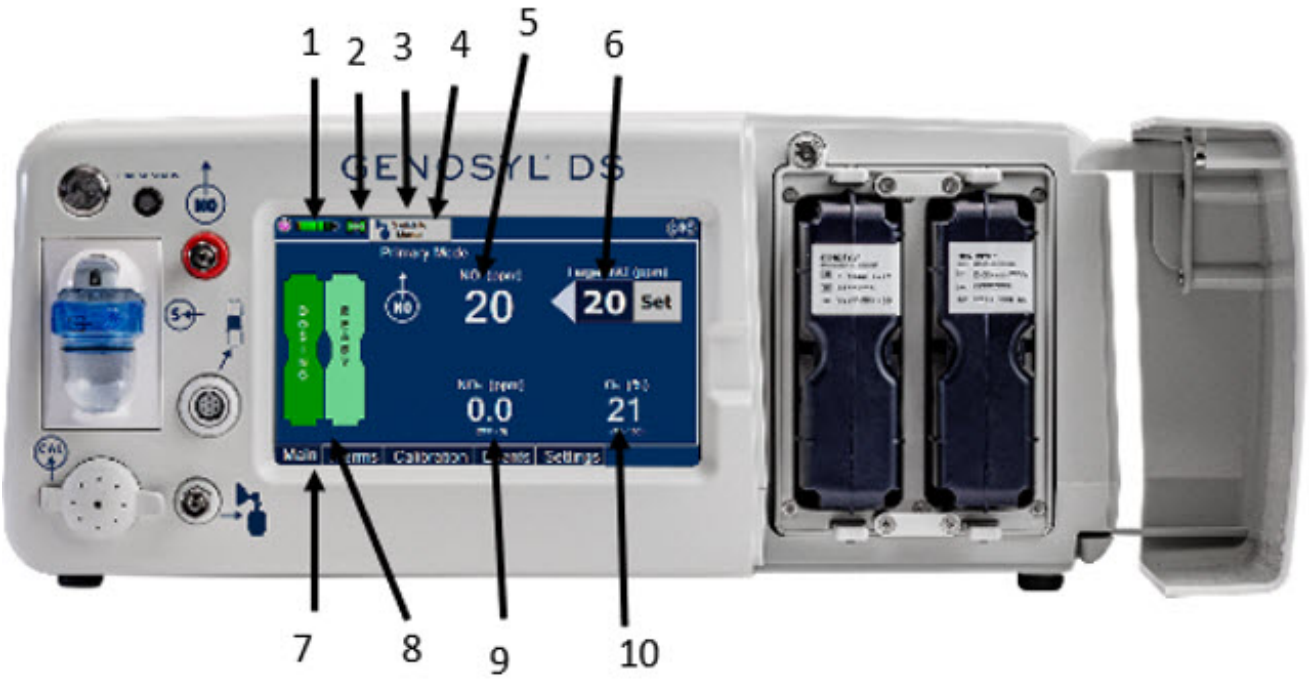


1. Silver Power Button
2. Battery Charge Indicator
3. NO Delivery Port
4. Water Trap with Gas Sample Port
5. Calibration Port
6. Manual Ventilation Port
7. Adaptive Sensor Port
8. Dual Cassettes
9. Cassette Access Door



1. Battery Charge Status Indicator
2. Adaptive Sensor Indicator
3. Mode Switch Button
4. Console Mode
5. Measured NO Dose (ppm)
6. Target NO Dose (ppm)
7. Menu Tab
8. Dual Cassette Status Indicator
9. NO_2 Measured Level (ppm)
10. O_2 Measured Level (ppm)

1. SYSTEM SET-UP AND CONNECTIONS

1.1. GENOSYL DS Set-Up and Mechanical Ventilator Circuit Schematic

NOTE: Naming conventions: The GENOSYL DS accessories and components consist of the GENOSYL Injection Assembly with Adaptive Sensor or GENOSYL DS Mixer Assembly with Adaptive Sensor, and the GENOSYL DS Gas Lines. Refer to Section 6.7 Table 5 for when use of the Mixer Assembly with Adaptive Sensor is recommended.

NOTE: All circuit components, including GENOSYL DS circuit components, should be changed out according to hospital protocol.

WARNING:

- ALWAYS use the GENOSYL DS in accordance with the indications, usage, contraindications, warnings, and precautions described in the GENOSYL prescribing information and labeling. Refer to latest approved prescribing information and labeling prior to use.
- The approved patient population for the GENOSYL DS as specified in the drug labeling for GENOSYL (nitric oxide) for inhalation, is limited to neonates. The GENOSYL DS is not intended to be used in other patient populations.
- ONLY use the GENOSYL DS, its parts, and accessories as instructed. Using non-specified components may result in product malfunction, injury or death.

- ALWAYS follow pre-use setup instructions for the routing and connections of tubing to avoid patient strangulation.
- MAKE SURE the System has all tubing connected as described in the instructions. Not connecting all tubing may result in inaccurate dosage and harm to the patient.
- DO NOT use accessories or cables other than those specified or provided by the manufacturer of this equipment, as this may result in increased electromagnetic emissions or decreased electromagnetic immunity of this equipment and result in improper operation.

1.2. Connections to Various Breathing Systems

1.2.1. **Conventional Ventilators**

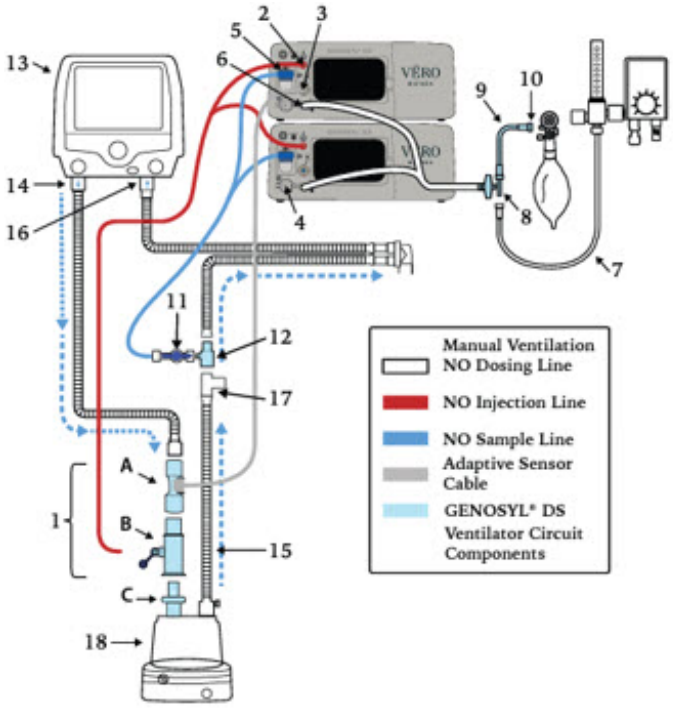
- Bio-Med Devices CrossVent 2+/2i+
- Bio-Med Device MVP-10
- Dräger V500
- Dräger VN500
- GE Healthcare R860
- Hamilton C1/T1
- Hamilton C2/C3
- Hamilton G5
- Hamilton MR1
- Maquet Servo-U/N/I
- Maquet Servo-I MR
- Puritan Bennett 840
- Puritan Bennett 980
- Vyaire AVEA

WARNING:ONLY use the GENOSYL DS with Bio-Med Crossvent 2+/2i+ with Constant Flow ON. Not doing so may lead to elevated NO2 levels or dose variability.

Table 1: Conventional Ventilator Compatibility Test Ranges

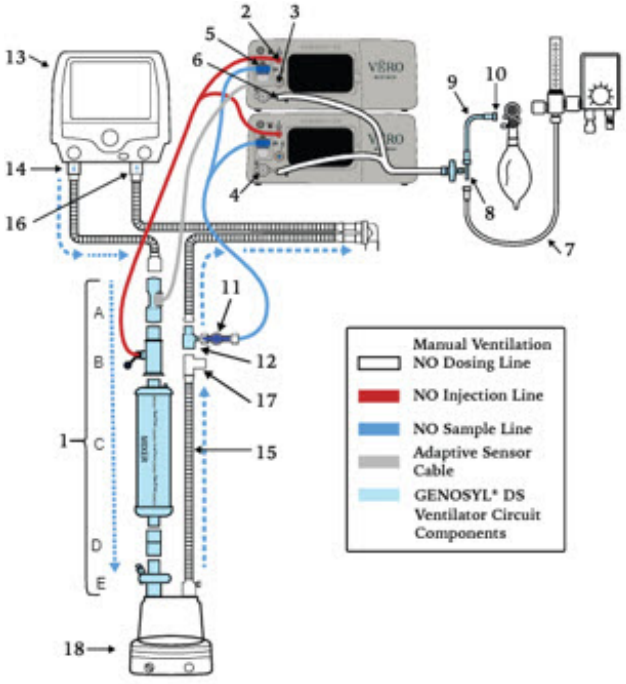
Setting	Range	Unit
Inspiratory Flow Rate	2-120	LPM
Respiratory Rate	6-60	BPM
Peak Inspiratory Pressure	0-70	cmH_2O
PEEP	0-20	cmH_2O

For applicable use scenarios, and when use of a mixer is required, see Section 6.7, Table 5**.**



1. Injection Assembly with Adaptive Sensor*
   - A. Adaptive Sensor
   - B. NO Gas Injection Adapter
   - C. Inline Breating Circuit Filter
2. GENOSYL (nitric oxide) Port
3. Adaptive Sensor Port
4. Calibration Port
5. Water Trap
6. Manual Ventilation NO Dosing Port
7. Oxygen Tubing
8. Oxygen Tubing Connection with Filter
9. Manual Ventilation Bag NO Adapter
10. Manual Ventilation Bag Connector
11. Stopcock
12. Gas Sample Tee
13. Ventilator
14. Ventilator Inspiratory Outlet
15. Inspiratory Limb
16. Ventilator Expiratory Inlet
17. Temperature Port Probe
18. Humidifier

*See Section 1.4.1 for detailed assembly instructions for the Injection Assembly with Adaptive Sensor



1. Mixer Assembly with Adaptive Sensor*
   - A. Adaptive Sensor
   - B. NO Gas Injection Adapter
   - C. Mixer
   - D. Adapter (22F X 22F)
   - E. Inline Breathing Circuit Filter
2. GENOSYL (nitric oxide) Port
3. Adaptive Sensor Port
4. Calibration Port
5. Water Trap
6. Manual Ventilation NO Dosing Port
7. Oxygen Tubing
8. Oxygen Tubing Connection with Filter
9. Manual Ventilation Bag NO Adapter
10. Manual Ventilation Bag Connector
11. Stopcock
12. Gas Sample Tee
13. Ventilator
14. Ventilator Inspiratory Outlet
15. Inspiratory Limb
16. Ventilator Expiratory Inlet
17. Temperature Port Probe
18. Humidifier

*See section 1.4.2 for detailed assembly instructions for the Mixer Assembly with Adaptive Sensor

1.2.2 Non-Invasive Gas Delivery Systems

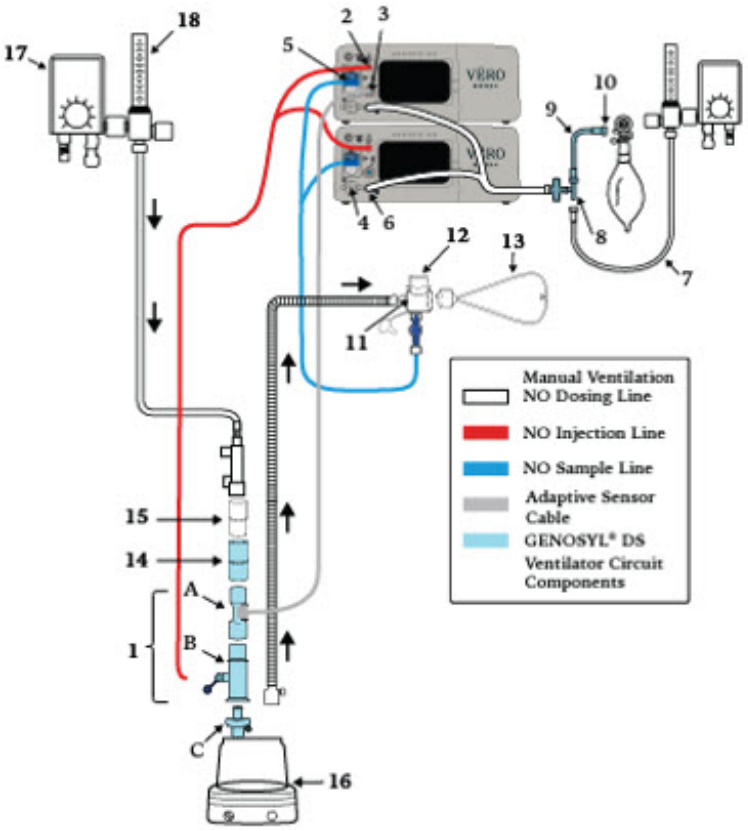
- Fisher and Paykel Optiflow Jr Breathing Circuit
- Fisher and Paykel Optiflow Breathing Circuit
- Infant Bubble Continuous Positive Airway Pressure (CPAP)

Table 2: Non-Invasive Gas Delivery System Compatibility Test Ranges

Setting	Range	Unit

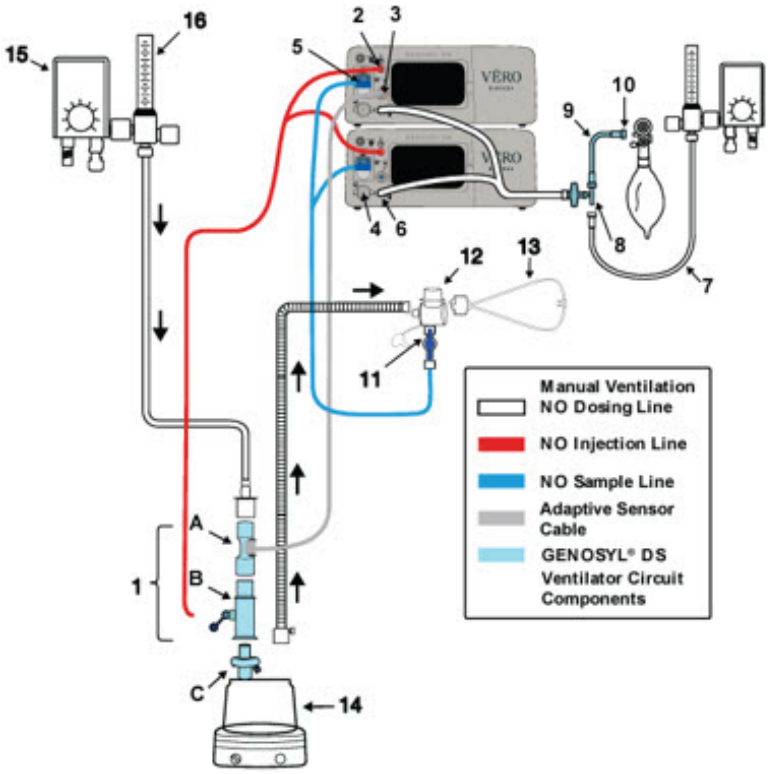
Fisher and Paykel Optiflow Jr Breathing Circuit	0.75-36	LPM
Fisher and Paykel Optiflow Breathing Circuit	3-60	LPM
Bubble CPAP Continuous Flow Rate	4-15	LPM
CPAP Pressure	3-10	cmH $_2$O

For applicable use scenarios, see Section 6.7, Table 5.



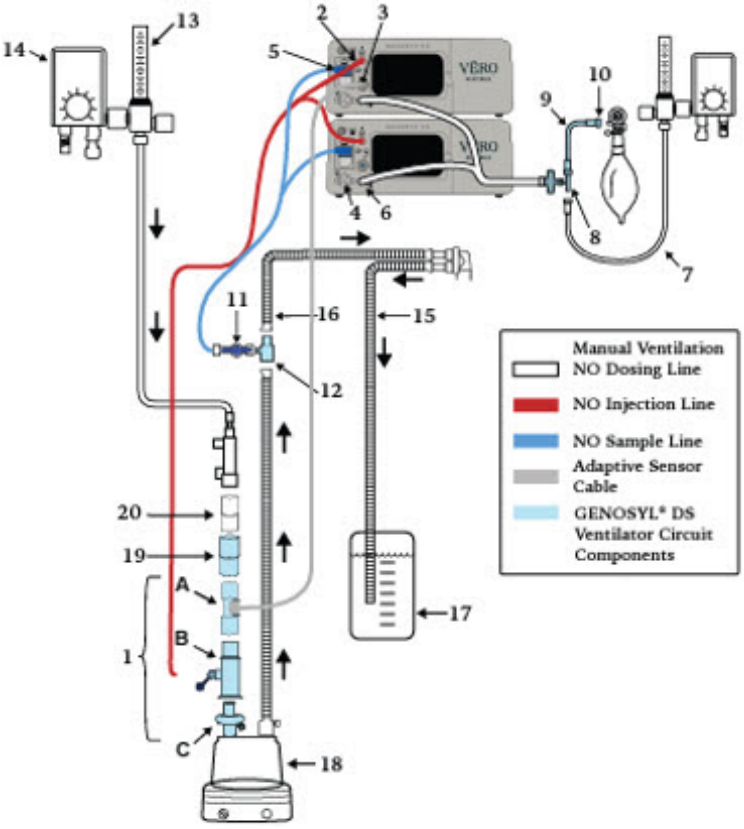
1. Injection Assembly with Adaptive Sensor*
   - A. Adaptive Sensor
   - B. NO Gas Injection Adapter
   - C. Inline Breathing Circuit Filter
2. GENOSYL® (nitric oxide) Port
3. Adaptive Sensor Port
4. Calibration Port
5. Water Trap
6. Manual Ventilation NO Dosing Port
7. Oxygen Tubing
8. Oxygen Tubing Connection with Filter
9. Manual Ventilation Bag NO Adapter
10. Manual Ventilation Bag Connector
11. Stopcock
12. Optiflow Jr Adapter (REF OPT016)
13. Optiflow Jr Cannula
14. Adapter (22F X 22F)
15. Adapter (22M X 22M)
16. Humidifier
17. Air /Oxygen Blender
18. Flowmeter

*See Section 1.4.1 for detailed assembly instruction for the Injection Assembly with Adaptive Sensor



1. **Injection Assembly with Adaptive Sensor***
   A. **Adaptive Sensor**
   B. **NO Gas Injection Adapter**
   C. **Inline Breathing Circuit Filter**
2. **GENOSYL® (nitric oxide) Port**
3. **Adaptive Sensor Port**
4. **Calibration Port**
5. **Water Trap**
6. **Manual Ventilation NO Dosing Port**
7. **Oxygen Tubing**
8. **Oxygen Tubing Connection with Filter**
9. **Manual Ventilation Bag NO Adapter**
10. **Manual Ventilation Bag Connector**
11. **Stopcock**
12. **Optiflow Jr Adapter (REF OPT016)**
13. **Optiflow Cannula**
14. **Humidifier**
15. **Air/Oxygen Blender**
16. **Flowmeter**

*See Section 1.4.1 for detailed assembly instructions for the Injection Assembly with Adaptive Sensor



1. Injection Assembly with Adaptive Sensor*
   A. Adaptive Sensor
   B. NO Gas Injection Adapter
   C. Inline Breathing Circuit Filter
2. GENOSYL (nitric oxide) Port
3. Adaptive Sensor Port
4. Calibration Port
5. Water Trap
6. Manual Ventilation NO Dosing Port
7. Oxygen Tubing
8. Oxygen Tubing Connection with Filter
9. Manual Ventilation Bag NO Adapter
10. Manual Ventilation Bag Connector
11. Stopcock
12. Gas Sample Tee
13. Flowmeter
14. Air/Oxygen Blender
15. Expiratory Limb
16. Inspiratory Limb
17. Bubble Jar
18. Humidifier
19. Adapter (22F X 22F)
20. Adapter (22M X 22M)

*See Section 1.4.1 for detailed assembly instructions for the Injection Assembly with Adaptive Sensor

1.3 GENOSYL DS Ventilator Circuit Assembly Pre-Check

Follow the steps listed below for the initial System pre-check prior to completing the ventilator circuit assembly.

1. Removeall items of the GENOSYL DS Parts / Components from packaging.

2. Checkthe expiration date for each Cassette and Inline Breathing Circuit Filter(if Mixer assembly is used) to ensure use is within the expiration date.

WARNING:DO NOT use a Cassette that is beyond its expiration date. Using an expired Cassette may affect the Cassette's ability to provide the correct NO dosage to the patient, which may cause injury or death.

1. Visually inspectthe Water Traps on both Consoles to ensure they are installed and empty (Note: To empty the Water Trap, see Section 6.3.1).

WARNING:

- ALWAYS empty Water Trap before each use, when prompted by the System, and when the trap is more than half full. Allowing the Water Trap to completely fill will occlude the Sample Line which will interrupt patient gas NO, NO_2, and O_2concentration monitoring. Failure to monitor the patient gas NO, NO_2, and O_2concentrations may result in patient injury.
- ALWAYS conduct Water Trap/Sample Line Leak Test every time you empty and replace the Water Trap, as failure to do so may lead to an incorrect NO reading, which can result in injury or death.

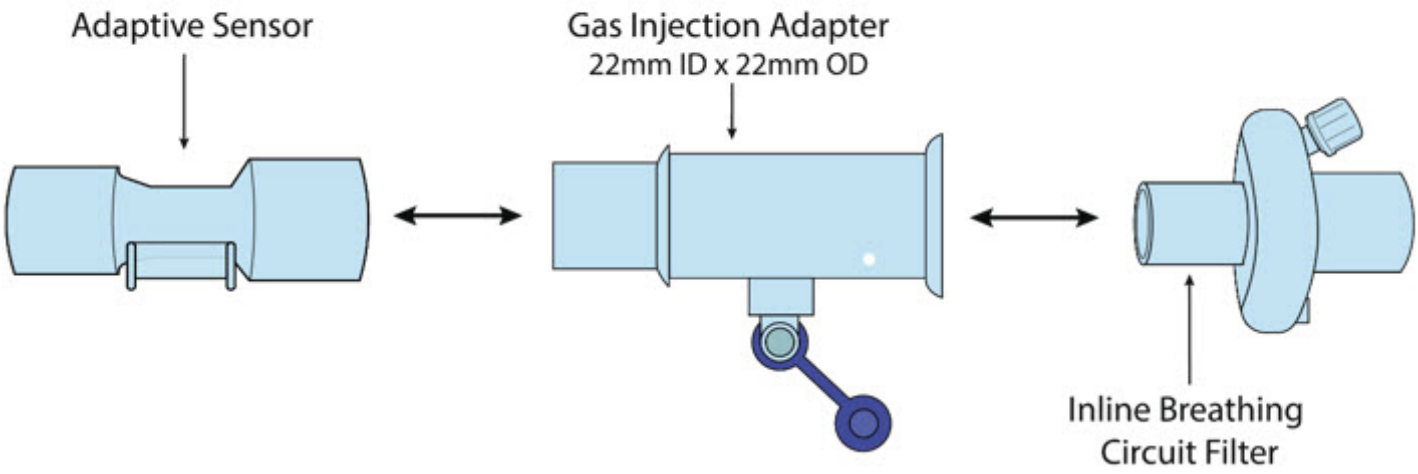
1.4 Assembling GENOSYL DS Injection Assembly with Adaptive Sensor

The Injection Assembly with Adaptive Sensor or the Mixer Assembly with Adaptive Sensor is the point of Nitric Oxide injection into the patient respiratory circuit. Only one type assembly is required for each patient circuit. For certain scenarios, the Mixer Assembly with Adaptive Sensor is recommended to mix the NO gas with the gas supplied by the ventilator through a filter containing silica gel to provide intra-breath NO delivery. Refer to Table 5 for scenarios when a Mixer is recommended for use.

NOTE: When using a Mixer, an Inline Breathing Circuit Filter must be used. If a Mixer is not used, an Inline Breathing Circuit Filter as presented in Figure 8may be used, or an Injection Line Filter connected to the port on the Gas Injection Adapter may be used.

1.4.1 GENOSYL DS Injection Assembly with Adaptive Sensor

1. Connectthe Inline Breathing Circuit Filter to the Gas Injection Adapter (22mm ID × 22 mm OD).
2. ConnectAdaptive Sensor to the inlet end of Gas Injection Adapter.

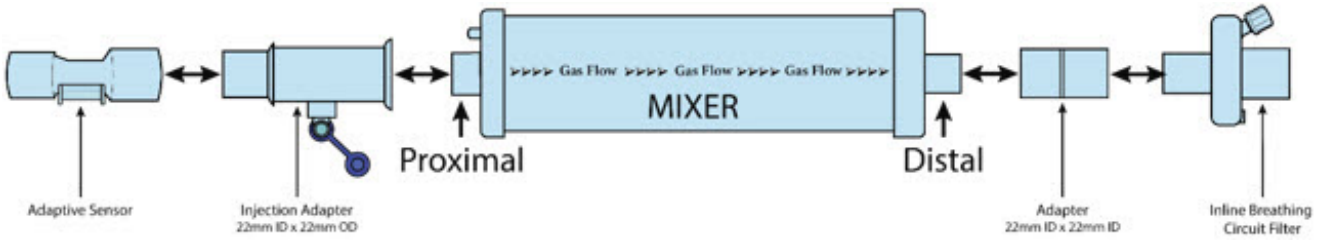


1.4.2 GENOSYL DS Mixer Assembly with Adaptive Sensor

1. Connectthe Inline Breathing Circuit Filter to the Gas Injection Adapter (22mm ID × 22 mm OD).
2. Connectthe Gas Injection Adapter (22mm ID × 22 mm OD) to the distal end of the Mixer.
3. Connectthe Gas Injection Adapter to the proximal end of the Mixer.

1. ConnectAdaptive Sensor to the proximal end of the Gas Injection Adapter.

NOTE: Ensure the Sample Lines are connected to the **Water Traps on both Consoles.**



NOTE: To determine if the Injection Assembly with Adaptive Sensor or the Mixer Assembly with Adaptive Sensor is recommended, see Section 6.7, Table 5.

1.5 GENOSYL DS Console Connections

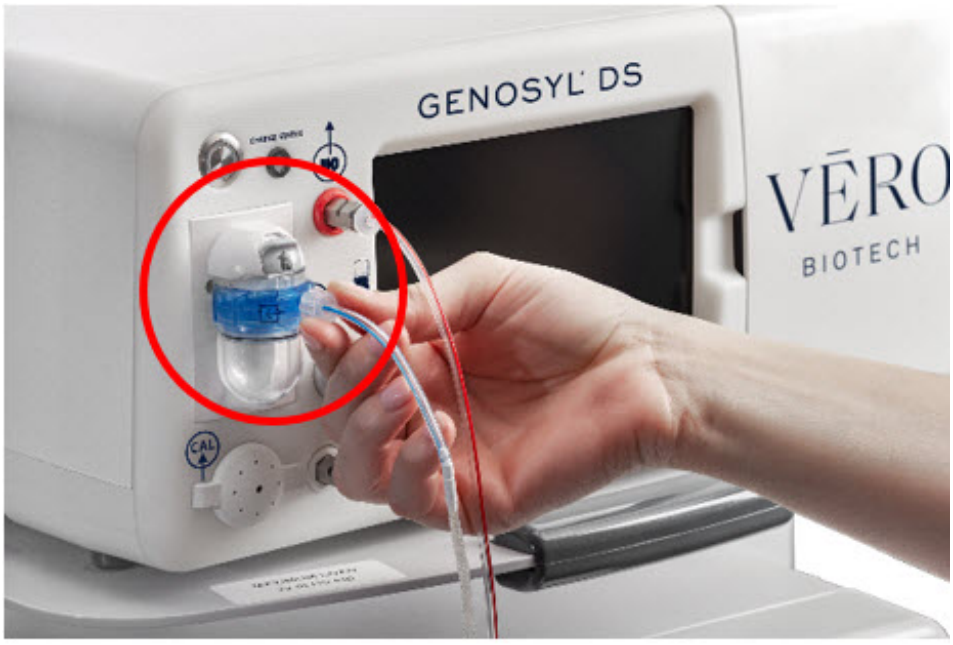
1.5.1 GENOSYL DS Gas Lines Connections

Follow the steps listed below to connect the Gas Lines to both Consoles.

1. Pushand twistclockwise the short Y-end of the NO Injection Line (red) to the "NO" port on the front panel of the top Console.

1. Pushand twistthe short Y-end of the Sample Line (blue) to the Gas Sample Port on the front of the Water Trap, attached to the top Console.

NOTE: Ensure the Sample Lines are connected to the **Water Traps on both Consoles.**

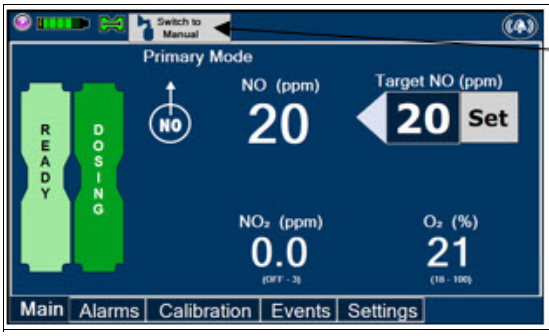


1. Pushand twistthe short Y-end of the Manual Ventilation Line (clear) to the Manual Bagging Port on the front of the top Console.

1. Repeatsteps 1, 2, and 3 on the bottom Console.
2. ConnectAdaptive Sensor Cable to Adaptive Sensor Port on front of the Primary Console.

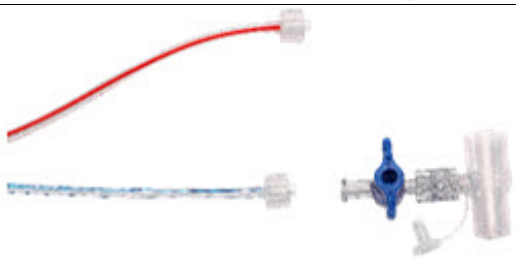
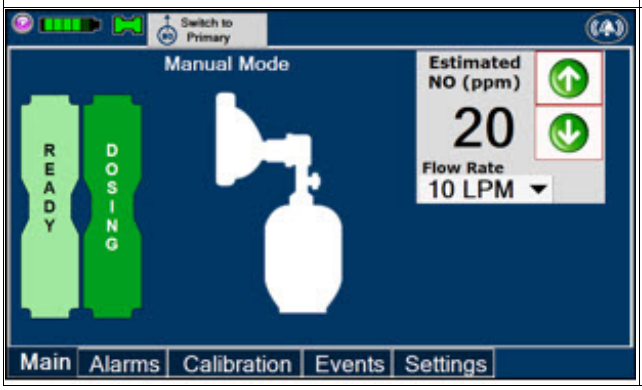
1.5.2 GENOSYL DS Sample Line Extension Connection

For use in the MR Environment when a longer sample line may be required, follow the steps listed below to connect a Sample Line Extension. It is recommended to install the extension prior to initiation of dose.



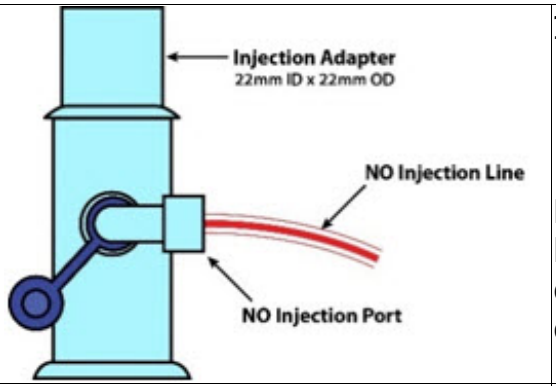
1. If actively dosing, switchto Manual prior to completing the following steps.

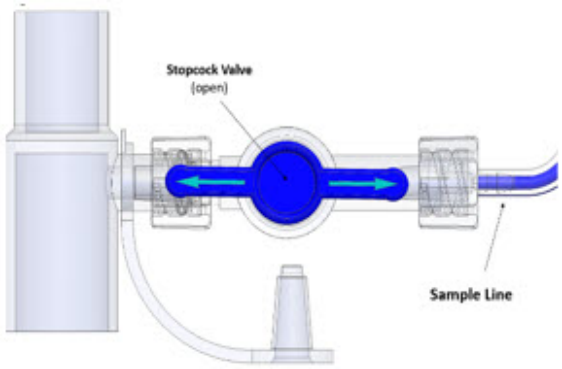
WARNING: Failure to switch to Manual Mode prior to installing a Sample Line Extension when the System is actively dosing may result in a spike in the NO dose delivered to the patient.

	1. Turnthe blue Stopcock Valve, attached at the Gas Sample Tee, to the closed position as shown.
	1. Pushand twistcounterclockwise the Luer-Lock Collar of the Sample Line to remove from the blue Stopcock Valve at the Gas Sample Tee.
	1. Pushand twistclockwise the Luer-Lock Collar of the Sample Line onto the Sample Line Extension female connection. 2. Pushand twistclockwise the Luer-Lock Collar of the Sample Line onto the blue Stopcock Valve at the Gas Sample Tee. 3. PerformWater Trap/Sample Line Leak test, as instructed.
	1. If actively dosing, switchback to Primary Mode

1.5.3 GENOSYL DS Respiratory Circuit Connections

Follow the steps listed below to connect the Gas Lines to the Injection Assembly, Sample Tee, and Adaptive Sensor. If a Sample Tee already exists within the ventilator circuit, the Sample Line may be connected directly to the existing Sample Tee.

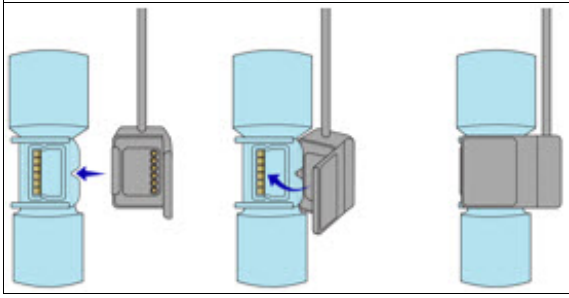
	1. Pushand twistclockwise the Luer-Lock Collar from the NO Injection Line onto the NO Injection Assembly. **NOTE:**After connecting, the valve assembly may have rotated such that the orientation may appear different from what is shown here and on the display screen.



1. Pushand twistclockwise the Luer-Lock Collar of the Sample Line onto the Sampling Port of the Gas Sample Tee.

NOTE: Skip this step if a Gas Sample Tee is already connected and in-line with the ventilator circuit.

1. Ensurethe blue Stopcock Valve is in the open position as shown.



1. Connect the distal end of the Adaptive Sensor Cable to the Adaptive Sensor on the Injection Assembly

1.6.1 Manual Ventilation (Bag) Connection

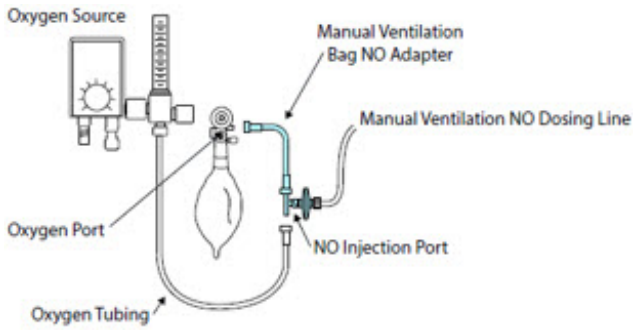


Figure 10: Manual Ventilation System

1. Attachthe barbed end of the Manual Ventilation Bag NO Adapter into the oxygen tubing from the oxygen source.
2. Attachthe other end of the NO Adapter to the oxygen port on the side of the Manual Ventilation Bag.
3. Connectthe Manual Ventilation Line (clear) to the NO Injection Port of the Manual Ventilation Bag NO Adapter.
4. Placethe Manual Ventilation Assembly in a clean accessible place if needed for future use.

1.7 Mechanical Ventilator Circuit Connections

Follow the steps outlined in this section to connect the GENOSYL DS Ventilator Circuit Assembly to the Mechanical Ventilator Circuit.

WARNING:

- ALWAYS ensure the trigger sensitivity of the ventilator is checked after connecting the GENOSYL DS to the breathing circuit. The GENOSYL DS injects and samples gas from the patient respiratory circuit which may affect the triggering sensitivity of the ventilator.
- ALWAYS ensure the patient disconnect and high–pressure alarms are used with the ventilator. Otherwise, the System is not working properly.

NOTE: All ventilator connections should be assembled and inspected prior to connecting to the mechanical ventilator circuit.

1. **Disconnect**the Inspiratory Tubing from the humidifier and attach it to the proximal end of the Injection Assembly to the Adaptive Sensor.
2. **Attach**the distal end of the Injection Assembly to the humidifier.
3. **Insert**the Sample Tee into the ventilator circuit at the proximal end of the temperature probe **closest to the patient.**

2 SYSTEM START UP

2.1 Console Start-Up

CAUTION:
- ONLY use the GENOSYL DS with the power cord supplied by the manufacturer. Use of a generic power cord may cause output voltage instability leading to a touch screen failure.
- ALWAYS ensure the power cord is firmly seated into the power supply and the wall outlet. A loose connection can result in damage to the device or faulty operation.

1. Pushthe Circular Power Connectors into the back of the top and bottom Consoles.
2. Connectthe main power cord to a grounded 120 V electrical outlet.
3. Pressthe Black Rocker Power Switch, located on the back of each Console, to the right (ON position) to power on both Consoles.
4. Pressthe Silver Power Button, located at the top left corner on the front panel **of each**Console, to turn on the display screens on both Consoles. The display screen will illuminate, and the Consoles will beep, indicating the power is on.

CAUTION: The System will conduct an internal self-test. If an alarm or failure message should occur, refer to Section 8 in the Operator's Manual to resolve the issue.

NOTE: If the display screen does not turn on, see Troubleshooting, Section 8of the Operator's Manual.

2.2 Cassette Insertion & Water Trap / Sample Line Leak Test

The following steps should be taken on both the top and bottom Consoles. Upon the insertion of the Cassette, a test will be initiated on each Console to check and ensure the integrity of the Water Traps and Sample Line.

The Water Trap / Sample Line Leak Test is **automatically initiated when a Cassette has been inserted,**and the measured NO is less than 1.0 ppm.

WARNING:ALWAYS follow Cassette insertion instructions prior to Cassette insertion. Not inspecting the Cassette prior to insertion may lead to using a faulty Cassette, resulting in injury.

1. Confirmthe Cassette State Window on each Cassette is blue.

WARNING:DO NOT use the Cassette if the Cassette State Window is not blue. A Cassette State Window that is any color other than blue may affect the Cassette's ability to provide the correct NO dosage to the patient, which may cause injury or death.

NOTE: If the Cassette State Window is not blue, see Troubleshooting, Section 8.7of the Operator's Manual.

1. Openthe Cassette Access Doors and insertttwo Cassettes into the Dosing Console and at least one Cassette into the Back-Up Console. Push until it clicks.

NOTE: The Water Trap / Sample Line Leak Test is **automatically initiated when a Cassette has been inserted,**and the measured NO is less than 1.0 ppm
After the first Cassette is fully inserted, **the Operator will have 60 seconds to close the blue Stopcock Valve**to perform the test.

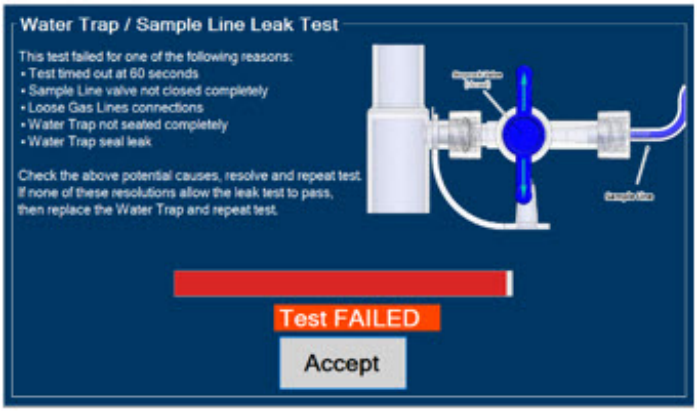
1. Followthe onscreen instructions **on both Consoles.**

NOTE:
- The screen will indicate the Water Trap / Sample Line Leak Test has started and the progress bar will be red until the stopcock valve has been closed, upon which it will then turn green if there is no leak detected.
- See Section 3.5for detail around dosing in Manual Mode.

1. Followthe onscreen instructions **on both Consoles.**

CAUTION: Open the blue Stopcock Valve priorto pressing "Accept". Failure to do so will result in a line occlusion error.

NOTE: If the Water Trap / Sample Line Leak Test fails, follow the onscreen instructions to resolve the issue. Also see Troubleshooting, Section 8.7of the Operator's Manual.



1. If this screen is displayed, followthe onscreen instructions on both Consoles
.
2. PressYes on both Consoles to begin a new Water Trap / Sample Line Leak Test.

3 NITRIC OXIDE ADMINISTRATION

3.1 Cassette Activation

3.2 Nitric Oxide Dose Set-Up and Administration

WARNING:

- MAKE SURE the System stabilizes to the prescribed concentration (ppm) of NO prior to leaving the Console unattended. Failure to do so could result in under delivery of the target NO, leading to injury or harm.
- ALWAYS constantly monitor the patient. System malfunctions can occur if device and patient are not monitored and can result in injury or death. Careful monitoring is required by care personnel whenever the System is used on a patient. The use of an alarm and a monitoring system does not give an absolute assurance of warning for every malfunction that may occur. Certain alarms may require immediate response.
- If the gas flow of the patient's respiratory device/ventilator should be interrupted or discontinued, the NO dose should be maintained by switching to Manual Mode or the target NO dose should be set to zero.

3.3.1 Setting a dose when using a circuit with an Adaptive Sensor

1. Pressthe gray "Set" button on the display screen.
2. Enterthe prescribed dose in ppm on the electronic keypad.
3. PressOK to confirm the entry.

3.3.2 Setting the dose when using a circuit without an Adaptive Sensor

1. Pressthe gray "Set" button on the display screen.
2. ConfirmTotal Flow Range is appropriately selected.
3. Enterthe prescribed dose in ppm on the electronic keypad.
4. PressOK to confirm the entry.

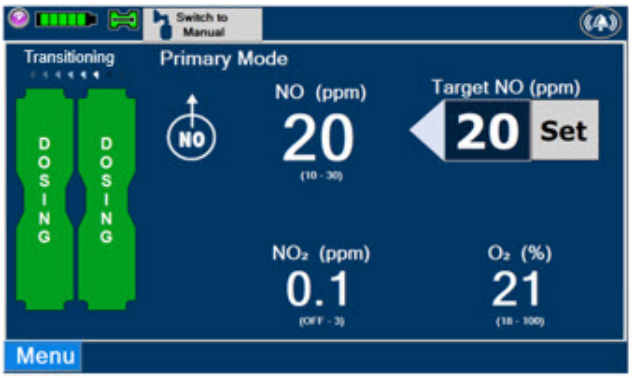
NOTE:

- The time to reach target dose may vary up to 10 minutes.
- If unable to set the dose in Primary Mode, see Troubleshooting, Section 8of the Operator's Manual.

3.3 Replacement of a Depleted Cassette

The GENOSYL DS automatically switches from the dosing Cassette to the secondary Cassette in the Dosing Console once the Cassette is depleted, when a secondary Cassette is properly inserted and preheated. After transition, the depleted Cassette is automatically ejected.

CAUTION:
User should always have a secondary Cassette inserted in Dosing Console and preheated in order for auto transition to occur. User should replace depleted Cassette as soon as possible after ejection.

ILLUSTRATION	ACTION	Warnings, Cautions and Notes
		**NOTE** The Console will automatically transition to the secondary Cassette if properly inserted and preheated. The screen to the left will be displayed during the transition process.

3.4 Manual Mode

NOTE: When entering Manual Mode, the set target dose in primary will carry over to Manual Mode if 5 ppm or greater. Less than 5 ppm set target dose in Primary will default to 5 ppm dose in Manual Mode. However, dose and flow rate be adjusted for specific situations. The feedback loop is disabled while in Manual Mode. To reinitiate the feedback loop, switch back to Primary Mode as soon as the situation permits

3.4.1 Manual Ventilation Use (Bagging)

WARNING:

- ALWAYS ensure that the manual flow displayed on the Console matches the flow set into the resuscitation bag. Incorrect flow settings may result in an incorrect estimation of NO delivery. If the flow into the manual equipment is too low, there is risk of overdosing the patient with NO.
- ALWAYS squeeze the bag several times, after starting fresh gas flow, to empty residual gas in the bag prior to using the System to ventilate a patient. Failure to do so could result in higher NO_2 levels being delivered to the patient.
- ALWAYS use the smallest bag adequate to deliver the desired tidal volume. Failure to do so could result in higher NO_2 levels being delivered to the patient.
- ONLY use a manual resuscitation bag with the GENOSYL DS for a short time (e.g., less than one hour) when on battery only. Otherwise, the System may shut off and may result in injury or death.
- If the dilution flow rate displayed on the screen does not match the wall source, then the estimated NO may be inaccurate.

1. Ensure the oxygen source is set appropriately or adjust as needed.
2. Press the button "Switch to Manual" on the Primary Console.
3. Press "Confirm" to switch to Manual Mode
4. To resume primary dosing, see Section 3.5.

NOTE:

- Dosing has been initiated at the default setting of 20 ppm at 10 LPM flow rate, however, these levels may be adjusted.
- If the dosing was set at "0" prior to pressing the "Switch to Manual" button, the estimated NO will also be at "0" and will need to be adjusted. If the primary dosing was set between 1 and 5 ppm prior to pressing the "Switch to Manual" button, the estimated NO dose will also be 5 ppm and may be adjusted.
- If an adjustment of the NO concentration is required, press the green up and down arrows.
- If an adjustment to the Dilution Flow Rate is required, press the LPM value and a drop-down menu will expand. Press the prescribed value. The new value will be highlighted in blue and the drop-down menu will collapse.

3.5 Resuming Primary Dosing

1. Pressthe "Switch to Primary" button at the top of the Manual Mode screen. This now becomes the Primary Console.
2. Press"Confirm" to start dosing or "Cancel" to cancel.

NOTE:

- The NO dose used in Manual Mode will become the set target dose in Primary Mode.

3.6 Adjusting the Dose

To adjust the dose of nitric oxide administered per hospital protocol/physician order. Follow the instructions listed below.

3.6.1 Adjusting the Dose when using a Circuit ***with*** an Adaptive Sensor

1. Pressthe gray "Set" button to access the electronic keypad on the display screen on the Dosing Console.
2. Enterthe prescribed (ppm) dose using the electronic keypad.
3. Press"OK" to confirm the dose and to start dosing administration.

3.6.2 Adjusting the Dose when using a Circuit ***without*** an Adaptive Sensor

1. Pressthe gray "Set" button to access the electronic keypad on the display screen on the Dosing Console.
2. Enterthe prescribed (ppm) dose using the electronic keypad.
3. Adjust Total Flow Range, if necessary.
4. Press"OK" to confirm the dose and to start dosing administration.

3.7 Console Use as a Back-Up

This section describes the process of activating the Cassette in the Back-Up Console. Delivery of NO will begin immediately upon Cassette activation.

WARNING: If the dilution flow rate displayed on the screen does not match the ventilator dilution flow, then the estimated NO may be inaccurate.

1. Press the "Set" button on the Back-Up Console which will display the NO dose numeric keyboard and Flow Section menu.
2. Confirm Dose and Total Flow range is appropriately selected.
3. Press "OK" to confirm entry
4. Connect Adaptive Sensor to the front of the new Dosing Console

NOTE:
- The default Total Flow range displayed will be <2.5 LPM unless otherwise selected by the user.
- The Back-Up Console is now the Primary Console.
- Dosing has been initiated at the default setting of 20 ppm.

4 CONSOLE SHUTDOWN AND CASSETTE DISPOSAL

WARNING:NEVER turn the rear power switch OFF until the System has gone through a controlled shutdown or instructed by VERO Technical Support. Turning the rear power switch OFF prematurely (e.g., while it is still in use) will immediately shut down the device. This may result in interruption in NO delivery to the patient, which may cause injury or death.

CAUTION:
- NEVER turn the rear power switch OFF until the System has gone through a controlled shutdown or instructed by VERO Technical Support. Turning the rear power switch OFF prematurely (e.g., while it is still in use) will immediately shut down the device and may cause improper operation upon restart.
- ALWAYS power down the GENOSYL DS Console and disconnect the power to the Console when not in use. Failure to do so may lead to permanent damage to the Console.

4.1 Console Shutdown

If the administration of NO must be stopped, then the dose level must be set to "0" and the Cassette must be removed prior to shutting down the Console.
1. Pressthe gray "Set" button to access the electronic keypad on the display screen.
2. Setthe dose to "0" using the electronic keypad.
3. Press"OK" to confirm the entry.
4. If the Settings Tab is not displayed, pressthe "Menu" tab to access the sub-level tabs.
5. Pressthe "Settings" tab on the display menu.
6. Pressthe red "System Shut Down" icon.
7. Press"Confirm" to confirm shutdown.
8. Waituntil the Console shuts down, the display screen appears blank, and the Console emits an audible beep.

NOTE: The Console will inert any remain contents from a dosing Cassette upon ejection

rendering it unusable. If a Cassette has only been preheated, and not used for dosing, the contents have not been inerted and it can still be used

1. Openthe Cassette Access Door.
2. Removethe Cassette by pulling the Cassette straight out.
3. Disposethe Cassette per hospital policy.
4. Pressthe Black Rocker Power Switch to the "OFF" position.

WARNING: NEVER turn the rear power switch OFF until the System has gone through a controlled shutdown or instructed by VERO Technical Support. Turning the rear power switch OFF prematurely (e.g., while it is still in use) will immediately shut down the device. This may result in interruption in NO delivery to the patient, which may cause injury or death.

CAUTION:

- NEVER turn the rear power switch OFF until the System has gone through a controlled shutdown or instructed by VERO Technical Support. Turning the rear power switch OFF prematurely (e.g., while it is still in use) may cause improper operation.
- ALWAYS power down the GENOSYL DS Console and disconnect the power to the Console when not in use. Failure to do so may lead to permanent damage to the Console.

1. Repeatsteps 1-12 for the other Console.

NOTE: If the System does not shut down, see Troubleshooting, Section 8of the Operator's Manual.

4.2 Cassette Disposal

Following use, any remaining Cassette liquid contents are purged into an inerting chamber that is built into the Cassette, where the contents are chemically neutralized, rendering the Cassette safe for disposal. When the Cassette liquid contents are emptied into the inerting chamber, the Cassette State Window on the front of the Cassette reddens and bleaches from its original blue color, indicating the Cassette is depleted. The Cassette can now be disposed of per hospital policy.

5 ALARMS, ALERTS, AND TROUBLESHOOTING

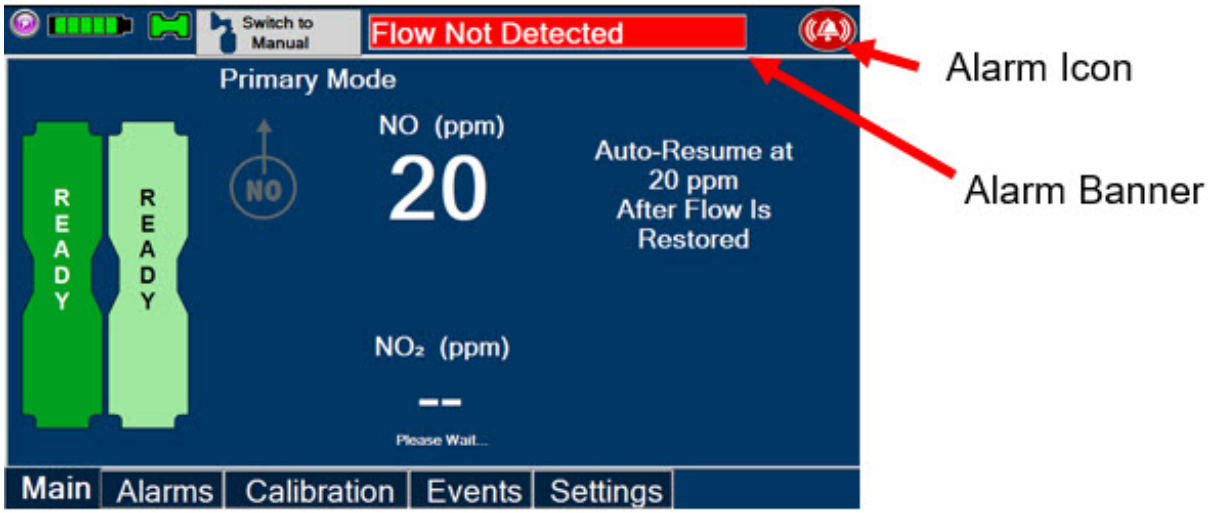
WARNING:ALWAYS ensure patient safety before troubleshooting (such as an activated alarm) or replacing a problematic item. Not monitoring the patient prior to attending to an alarm can result in injury or death.

5.1 Alarms, Alerts, and Troubleshooting

Section 8.1 of the **Operator's Manual**contains the system alarms and message in order of High (red), Medium (yellow), and Low Priority (cyan) followed by Informational

Messages (green). The table shows the alarm/symptom, the possible cause(s) of the alarm and recommended action to resolve the alarm. If the alarm/issue cannot be resolved, contact **Technical Support at 877-337-4118**.

A sample screen with an active alarm is shown below:



The alarm banner contains a drop-down menu containing a list of all alarms should there be multiple activated. The alarm icon is always present on the top right of the screen and tapping the icon will pre-silence or silence alarms. Refer the table below for descriptions of each alarm status:

ALARM ICON DISPLAY	DESCRIPTION
	No active alarm condition is detected on the Console. Tap this icon to activate the Pre-Silence feature.
	Alarms are actively pre-silenced. Countdown of time remaining appears under the icon. Pre-silence lasts for 120 seconds. Low/High NO, High NO_2, Low/High O_2, Water Trap Removed and Dosing Cassette Removed alarms are pre-silenced. Alarms will still be visible on alarm banner but audible alarm will not sound.
	Console has an active alarm condition that requires attention. Tap the icon to silence the alarm for 120 seconds.
	Console has an active alarm condition that requires attention and the alarms have been silenced. Countdown of time remaining appears under the icon.

6 MAINTENANCE

6.1 Calibration

WARNING:

- ONLY use the calibration gas pressure regulators supplied by the manufacturer.

Pressure regulators not supplied by the manufacturer may damage the sensors and may lead to patient injury.
- ALWAYS verify the correct NIST traceable calibration gas is being used and confirm the expiration date of the calibration gas prior to performing calibration. The use of incorrect or expired gas may result in inaccurate sensor readings and can lead to patient injury.
- NEVER perform NO or NO_2 calibration within the MR scanner room. Calibration equipment is a potential projectile hazard.

CAUTION:
- ALWAYS perform a full-scale calibration of the GENOSYL DS when prompted by the System prior to use.
- ALWAYS confirm the correct flow direction of the installed one-way check valve in the sampling tee to avoid over pressurization of the sampling system and damage to the device.

6.1.2 Air Calibration

Air Calibration will take up to 2 minutes. A progress bar is displayed in the lower left-hand corner of the display screen during the calibration process.

1. Checkto make sure nothing is connected to the CAL port during Air Calibration.
2. If the Calibration Tab is not displayed, pressthe "Menu" tab to access the sub-level tabs.
3. Pressthe "Calibration" tab on the display menu.
4. Pressthe Low Range "Air" button.
5. Pressthe blue "Start Calibration" button.
6. Press"OK" to continue once calibration is complete.

NOTE: If calibration fails, check if there is anything connected to the CAL port.

6.1.3 NO Calibration

WARNING:
- DO NOT open the valve prior to connecting to the CAL port. Opening the valve first will expose the user to NO gas.
- DO NOT interrupt calibration until finished. If interrupted, calibration will be cancelled.
- DO NOT disconnect tubing from the calibration port prior to closing the valve. Disconnecting the tubing first will expose the user to NO gas.

NOTE: NO calibration takes approximately 2 minutes. A progress bar is displayed in the lower left-hand corner of the display screen during the calibration process.

1. If the Calibration Tab is not displayed, pressthe "Menu" tab to access the sub-level tabs.

2. Pressthe "Calibration" tab on the display menu.
3. Pressthe High Range "NO" button.
4. Pressthe blue "Start Calibration" button.
5. Followthe onscreen instructions.
6. Press"OK" to continue once calibration is complete.

6.1.4 NO $_2$Calibration

WARNING:
- DO NOT open the valve prior to connecting to the CAL port. Opening the valve first will expose the user to NO $_2$gas.
- DO NOT interrupt calibration until finished. If interrupted, calibration will be cancelled.
- DO NOT disconnect tubing from the calibration port prior to closing the valve. Disconnecting the tubing first will expose the user to NO $_2$gas.

NOTE:NO $_2$calibration takes approximately 2.5 minutes. A progress bar is displayed in the lower left-hand corner of the display screen during the calibration process.

1. If the Calibration Tab is not displayed, pressthe "Menu" tab to access the sub-level tabs.
2. Pressthe "Calibration" tab on the display menu.
3. Pressthe High Range "NO $_2$" button.
4. Pressthe blue "Start Calibration" button.
5. Followthe onscreen instructions.
6. Press"OK" once calibration is complete.

6.2 Maintenance Schedule

The Console components require the following maintenance:

COMPONENT	SCHEDULE
Water Trap	Per patient or as required (per Leak Test)
Console	Yearly

The Console requires yearly factory service. The System will display an Information Message to remind the operator when service is required. Call **Technical Support at 877-337-4118**to schedule service.

6.3 Water Trap Maintenance

6.3.1 Emptying the Water Trap

WARNING:ALWAYS empty Water Trap before each use, when prompted by the System, and when the trap is more than half full. Allowing the Water Trap to completely fill will occlude the Sample Line which will interrupt patient gas NO, NO $_2$, and O $_2$concentration monitoring. Failure to monitor the patient gas NO, NO $_2$, and O $_2$concentrations may result in patient injury.

1. Remove Water Trap from Console by lifting latch and pulling the base of the Water Trap away from the Console.
2. Remove the lid by pulling the lid from the base.
3. Empty the liquid contents.
4. Clean the Water Trap per hospital policy and cleaning instructions in the Operator's Manual.
5. Reattach the lid by pushing it back onto base.
6. Slide the Water Trap back on the Console until it clicks into place.

6.3.2 Water Trap Replacement

WARNING:
- ALWAYS use a Water Trap supplied by the manufacturer. Using an incorrect water trap could result in non-functioning or inaccurate sensor readings.
- ALWAYS conduct a Water Trap test every time you empty and replace the Water Trap, as failure to do so may lead to an incorrect NO reading, which can result in injury or death.

If the Water Trap / Sample Line Leak Test does not meet requirements and the Sample Line integrity is confirmed or remains occluded, replace the Water Trap.
1. Remove old Water Trap from Console by lifting the latch and pulling the base of the Water Trap away from the Console.
2. Slide new Water Trap back on the Console until it clicks into place.
3. Discard the old Water Trap.

6.4 Battery

The battery will be serviced during scheduled maintenance performed by the manufacturer. If the need arises to replace the battery sooner than scheduled contact **Technical Support at 877-337-4118** to schedule a maintenance appointment.

During storage, the GENOSYL DS may be stored with the power off, but the external power supply should be connected at least once every 3 months to ensure a minimum charge is maintained on the internal battery.

WARNING: ONLY properly trained personnel should replace the battery. Incorrectly replacing the battery may result in a hazard such as excessive temperatures, fire, or explosion.

6.5 Cleaning

CAUTION:
- ALWAYS power down the GENOSYL DS Console and disconnect the power to the Console when not in use. Failure to do so may lead to permanent damage to the Console.
- DO NOT sterilize (e.g., autoclave, gas sterilize) any of the components of the System, as this may compromise performance.

- DO NOT use harsh cleaning agents on the GENOSYL DS. Doing so may impair the structural integrity and/or function of the device.
- ONLY use a damp cloth to clean the Console and limit use of liquids around Console. Excess water can permanently damage the device.
- ALWAYS ensure the System is completely dry after cleaning before powering it ON. Failure to do so could result in equipment damage.

6.5.1 Enclosure, Connections, and Surfaces Other Than the Display

Prior to performing any cleaning or maintenance operations ensure that the GENOSYL DS Console has been completely powered down and that the AC/DC power supply external to the GENOSYL DS Console has been unplugged. Apply any mild detergent to cloth prior to wiping down the System. Gently clean the outer surface of the unit with a soft damp cloth and mild detergent or isopropyl alcohol (70%).

WARNING:
- NEVER submerge the GENOSYL DS, Cassette, or non-disposable Adaptive Sensor Cable. Submerging in liquid will damage the System and could cause electrical shorts which may result in injury or death.
- DO NOT clean the GENOSYL DS with the power connected and the System turned ON, as this may lead to injury (e.g., shock). Unplug AC/DC power supply external to the System prior to cleaning.

6.5.2 Display Screen

Turn off Console and disconnect from AC power. Gently clean with a damp cloth.

CAUTION:
- DO NOT touch or rub the display screen with abrasive cleaning compounds or organic solvents, as they may scratch and damage the screen.
- DO NOT spray or pour liquids directly on the controller or the display, as they may damage the screen.

6.6 Storage

6.6.1 Cart / Console Storage

The acceptable storage conditions for the cart/Console are shown in the following table.

Cart / Console Storage	Temperature	-20°C to 60°C
	Humidity	15% to 95%, non-condensing
	Pressure	57kPa to 110kPa

During storage, the GENOSYL DS may be stored with the power off, but with the external power supply connected in which case the internal battery will be kept fully

charged.

During storage, the GENOSYL DS may be stored with the power off, but the external power supply should be connected at least once every 3 months to ensure a minimum charge is maintained on the internal battery.

WARNING:

- MAKE SURE the GENOSYL DS is connected to AC wall power to charge the battery a minimum of once every 3 months to maintain a minimum battery charge. Failure to recharge the Console battery for extended timeframes may result in full discharge of the battery. If a Battery Error message occurs during startup of the System, contact **Technical Support at 877-337-4118**for assistance.
- ONLY properly trained personnel should replace the battery. Incorrectly replacing the battery may result in a hazard such as excessive temperatures, fire, or explosion.
- ONLY store the GENOSYL DS as outlined in the storage instructions. Not storing the device in alignment with its storage instructions can cause the device to be unsafe and lead to injury or death.

6.6.2 Cassette / Accessory Storage

The GENOSYL DS may not function correctly if the Cassette or any of the System Accessories have been exposed to high levels of heat or humidity. Cassettes are supplied in a plastic container and should remain unopened until use. Cassettes should be stored at 25°C (77°F) with excursions permitted between 15°C to 30°C (59°F to 86°F). (See USP Controlled Room Temperature)

6.7 Ventilator Compatibility

The GENOSYL DS is compatible with the following equipment and accessories:

Table 3: Compatible Equipment and Accessories

MANUFACTURER	TYPE OF EQUIPMENT	MODEL
Fisher Paykel	Vent circuit kit	RT265
Fisher Paykel	Vent circuit kit	RT210
Fisher Paykel	Humidifier	850
Fisher Paykel	Humidifier Chamber	MR 290
Medline	Hyperinflated Resuscitator	Resus Hyperinf System 1/2L-LF
Laerdal	Self-inflated Resuscitator	Infant Silicone Resuscitators

Vero Biotech performs validation testing which determines the compatibility of ventilator/gas delivery systems with the GENOSYL DS. During this compatibility testing, the GENOSYL DS is evaluated for the following parameters while connected to each ventilator/gas delivery system:

- **NO Dose Accuracy:**Continuous and accurate delivery of a targeted dose of nitric oxide within ± 20% of setpoint or within +/- 2 ppm, whichever is greater.
- **Respiratory Device Gas Delivery and Alarms:**The respiratory device gas delivery device and alarms continue to function as intended by the manufacturer across the range of operating conditions.

- **NO_2 Performance:** NO_2 remains within acceptable limits less than 1.0 ppm with 60% FiO_2 and ≤40 ppm NO.
- **O_2 Dilution:** Post dilution O_2 level delivery is maintained within acceptable limits and conforms with the information presented in the GENOSYL DS Operator's Manual, Section 10.1.1, "Oxygen Dilution".
- **NO Concentration Transients:** NO concentration transients are ≤150% of mean concentration and as low as 0.0 ppm as long as the transient duration does not exceed 10% of the volumetric duration of the breath.

The testing performed demonstrated conformance with all specified requirements.

WARNING:

- ALWAYS use the GENOSYL DS in accordance with the indications, usage, contraindications, warnings, and precautions described in the GENOSYL prescribing information and labeling. Refer to latest approved prescribing information and labeling prior to use.
- The approved patient population for the GENOSYL DS as specified in the drug labeling for GENOSYL (nitric oxide) for inhalation, is limited to neonates. The GENOSYL DS is not intended to be used in other patient populations.

The following ventilators and non-invasive gas delivery systems have been validated for use with the GENOSYL DS. See Section 1for assembly instructions for Injection Assembly with Adaptive Sensor and Mixer Assembly with Adaptive Sensor.

Table 4: Details of Validated Systems

Manufacturer	Model	Neonatal	Pediatric/Adult	CPAP	HFNC	MR
Bio-Med Devices	Crossvent 2+/2i+	•	•			
Bio-Med Devices	MVP-10	•	•			
Dräger	VN500	•	•			
Dräger	V500	•	•			
GE Healthcare	R860	•	•			
Hamilton	C1/T1	•	•			
Hamilton	C2/C3	•	•			
Hamilton	MR1	•	•			•
Hamilton	G5	•	•			
Maquet	Servo-U/N/I	•	•			
Maquet	Servo-I MR	•	•			•
Puritan Bennett	840	•	•			
Puritan Bennett	980	•	•			
Vyaire Medical Inc.	AVEA	•	•			
Fisher & Paykel	Optiflow Jr Breathing Circuit				•	
Fisher and Paykel	Optiflow Breathing Circuit				•	
Fisher & Paykel	Bubble CPAP			•		

Fisher & Paykel	System					

Table 5: Validated Compatibility with and without Inline Mixer

See Section 1for assembly instructions for Injection Assembly with Adaptive Sensor and Mixer Assembly with Adaptive Sensor.

Manufacturer	Model	Ventilator Range Tested: Neonatal	Ventilator Range Tested: Pediatric/Adult	
		Ventilator Circuit using Injection Assembly with Adaptive Sensor (Without Inline Mixer)	Ventilator Circuit using Injection Assembly with Adaptive Sensor (Without Inline Mixer)	Ventilator Circuit using Mixer Assembly with Adaptive Sensor (With Inline Mixer)
Bio-Med Devices	Crossvent 2+/2i+	•	•	N/A
Bio-Med Devices	MVP-10	•	•	N/A
Dräger	VN500	•	•	N/A
Dräger	V500	•	VT < 400ml	VT > 400 – 600ml
GE Healthcare	R860	•	VT < 350ml	VT > 350 – 650ml
Hamilton	C1/T1	•	VT ≤ 450ml	VT > 450 – 600ml
Hamilton	C2/C3	•	VT ≤ 470ml	VT > 470 – 950ml
Hamilton	MR1	•	VT ≤ 470ml	VT > 470 – 950ml
Hamilton	G5	•	VT ≤ 950ml	VT > 950 – 1400ml
Maquet	Servo-U/N/I	•	VT ≤ 650ml	VT > 650 – 740ml
Maquet	Servo-I MR	•	VT ≤ 650ml	VT > 650 – 740ml
Puritan Bennett	840	•	VT < 300 mL	VT > 300-760 mL
Puritan Bennett	980	•	VT ≤ 485ml	VT > 485 – 1100ml
Vyaire Medical Inc.	AVEA	•	VT < 540ml	VT ≥ 540ml

Key:
• -Range Fully tested; use of Inline Mixer is not recommended
VT – Tidal Volume
VT Value listed – Tidal volumes in this range have been validated in accordance with column header

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Please read full prescribing information enclosed.
877.337.4118 | vero-biotech.com

PRINCIPAL DISPLAY PANEL - 216 L Cartridge Label

GENOSYL ®(nitric oxide) for inhalation

Recommended Dosage: See prescribing information.

For use with GENOSYL Delivery System only

LOT Z-XXXX-YYYY

SN ZZXXZXXX

EXP YYYY-MM-DD

Patents: http://www.vero-biotech.come/patents

Rx Only

800 PPM

NDC 72385-002-01

Bar Code

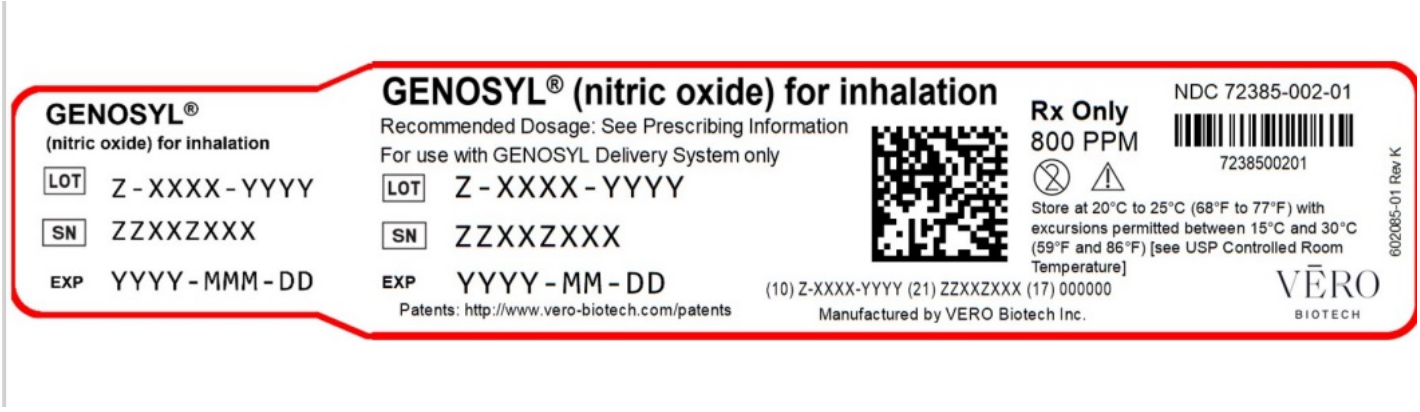
7238500201

Store at 20°C to 25°C (68°F to 77°F) with excursions permitted between 15°C and 30°C (59°F and 86°F) [see USP Controlled Room Temperature].

Manufactured by VERO Biotech Inc.

VĒRO
BIOTECH

602085-01 Rev K



GENOSYL

nitric oxide gas

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:72385-002
Route of Administration	RESPIRATORY (INHALATION)		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
NITRIC OXIDE (UNII: 31C4KY9ESH) (NITRIC OXIDE - UNII:31C4KY9ESH)	NITRIC OXIDE	0.98 mg in 1 L

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:72385-002-01	216 L in 1 CARTRIDGE; Type 0: Not a Combination Product	12/28/2022	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA202860	12/28/2022	

Labeler - VERO BIOTECH, INC. (872672477)

Registrant - VERO BIOTECH, INC. (872672477)

Establishment

Name	Address	ID/FEI	Business Operations
VERO BIOTECH, INC.		872672477	manufacture(72385-002)

Revised: 12/2024 VERO BIOTECH, INC.