US005558083A

United States Patent [19]

Bathe et al.

[11] **Patent Number: 5,558,083**

[45] **Date of Patent: Sep. 24, 1996**

[54] **NITRIC OXIDE DELIVERY SYSTEM**

[75] Inventors: **Duncan P. L. Bathe**, Madison; **Thomas S. Kohlmann**, McFarland; **John R. Pinkert**, Madison; **Robert Q. Tham**, Middleton, all of Wis.

[73] Assignee: **Ohmeda Inc.**, Liberty Corner, N.J.

[21] Appl. No.: **156,175**

[22] Filed: **Nov. 22, 1993**

[51] **Int. Cl.**[6] **A61M 15/00**

[52] **U.S. Cl.** **128/203.12**; 128/203.14; 128/203.25

[58] **Field of Search** 128/202.22, 203.12, 128/203.14, 203.25, 205.23

[56] **References Cited**

U.S. PATENT DOCUMENTS

4,127,121	11/1978	Westenskow et al.	128/203.14
4,191,952	3/1980	Schreiber et al.	128/203.14
4,328,823	5/1982	Schreiber	128/203.14
4,336,798	6/1982	Beran	128/205.23
4,345,612	8/1982	Koni et al.	128/203.14
4,442,856	4/1984	Betz	128/202.22
4,611,590	9/1986	Ryschka et al.	128/203.14
4,770,168	9/1988	Rusz et al.	128/203.14
5,159,924	11/1992	Cegielski et al.	128/203.25
5,197,462	3/1993	Falb et al.	128/203.14

FOREIGN PATENT DOCUMENTS

2121384	of 1994	Canada .
4325319	of 1994	Germany .
WO92/11052	of 1992	WIPO .
WO92/10228	of 1992	WIPO .

OTHER PUBLICATIONS

The Journal of Clinical Investigation, vol. 90, No. 2, Aug. 1992, pp. 421–428.

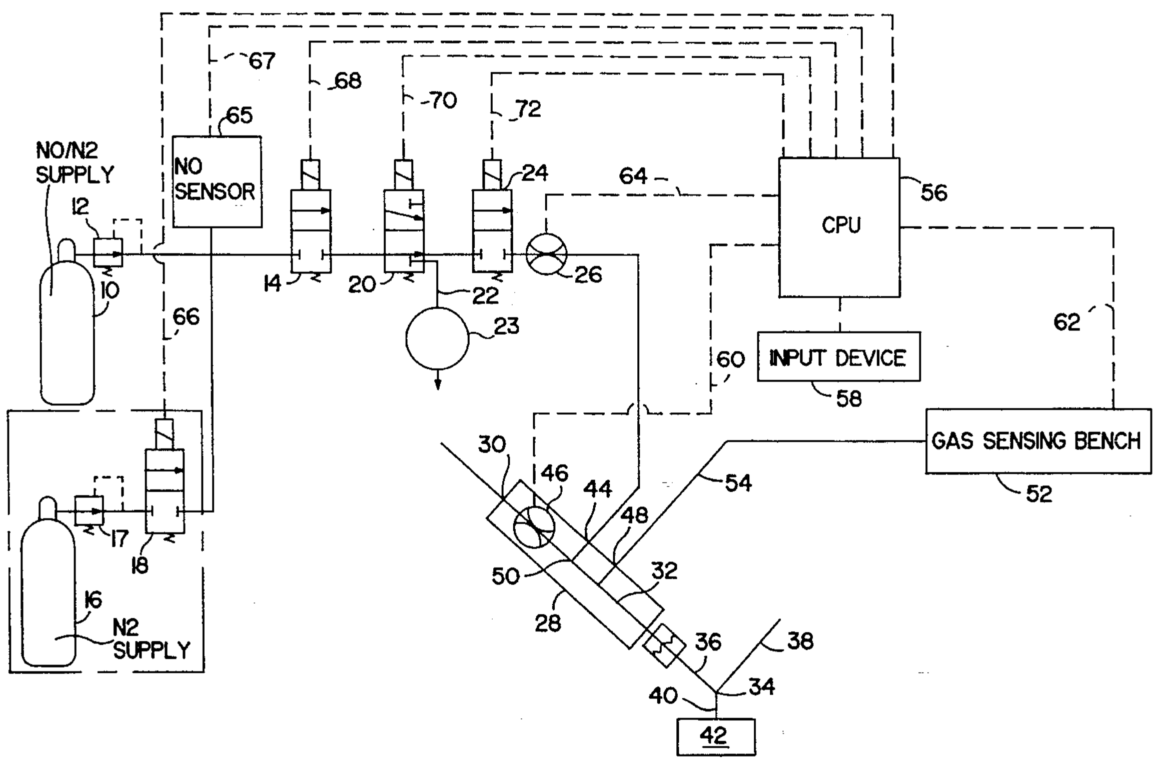
Primary Examiner—Aaron J. Lewis
Attorney, Agent, or Firm—Roger M. Rathbun; R. Hain Swope; Larry R. Cassett

[57] **ABSTRACT**

A nitric oxide delivery system that is useable with any of a variety of gas delivery systems that provide breathing gas to a patient. The system detects the flow of gas delivered from the gas delivery system at various times and calculates the flow of a stream of nitric oxide in a diluent gas from a gas control valve. The flow of gas from the gas delivery system and the flow established from the flow control valve create a mixture having the desired concentration of nitric oxide for the patient.

The system does not have to interrogate the particular gas delivery system being used but is an independent system that can be used with various flows, flow profiles and the like from gas delivery systems.

27 Claims, 2 Drawing Sheets



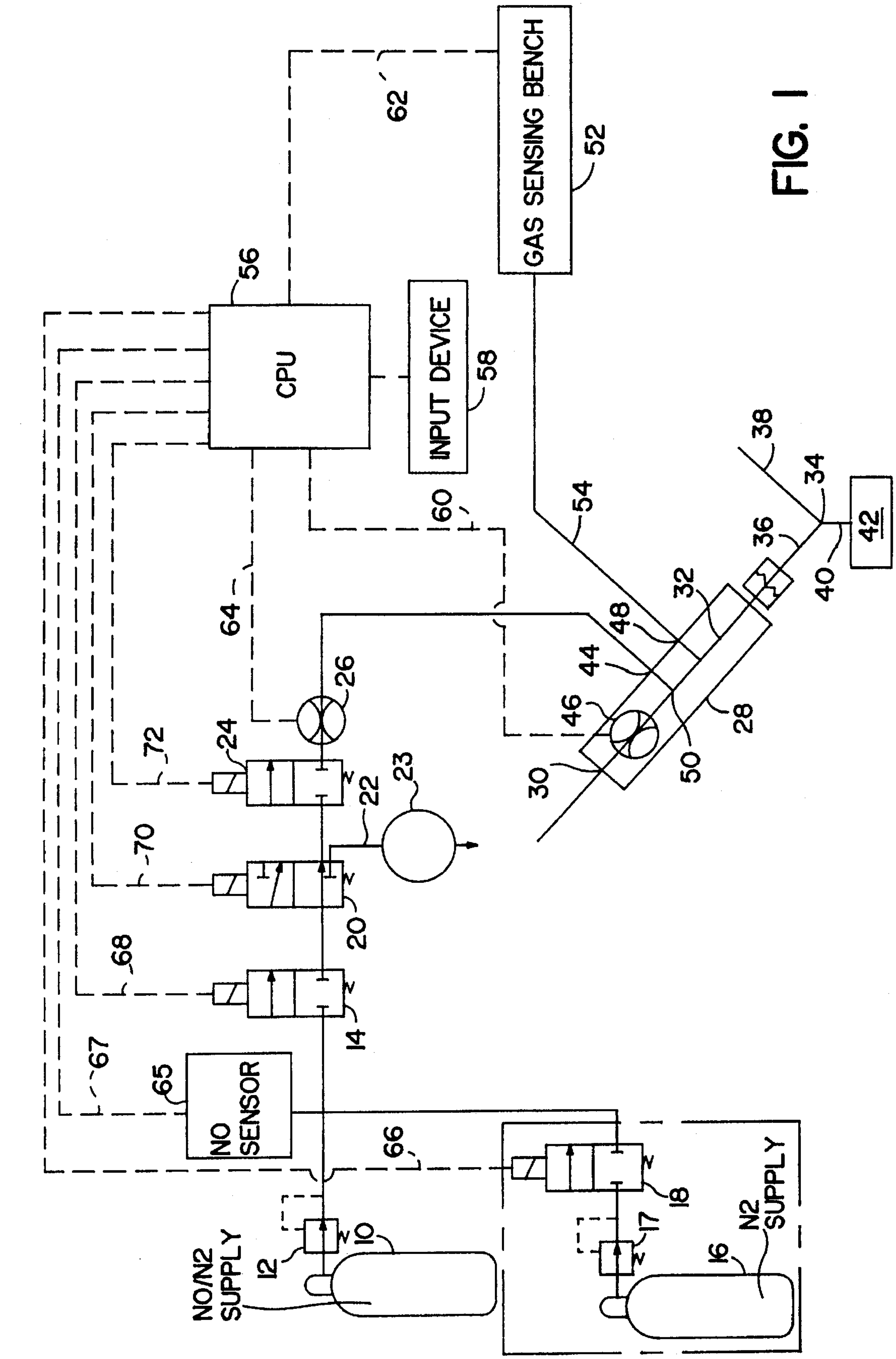

GAS SENSING BENCH
52
62
56
CPU
INPUT DEVICE
58
60
54
38
34
42
36
40
32
48
44
64
26
46
28
50
30
72
24
23
22
70
20
68
14
67
65
NO SENSOR
66
18
NO/N2 SUPPLY
12
10
17
N2 SUPPLY
16

FIG. 1

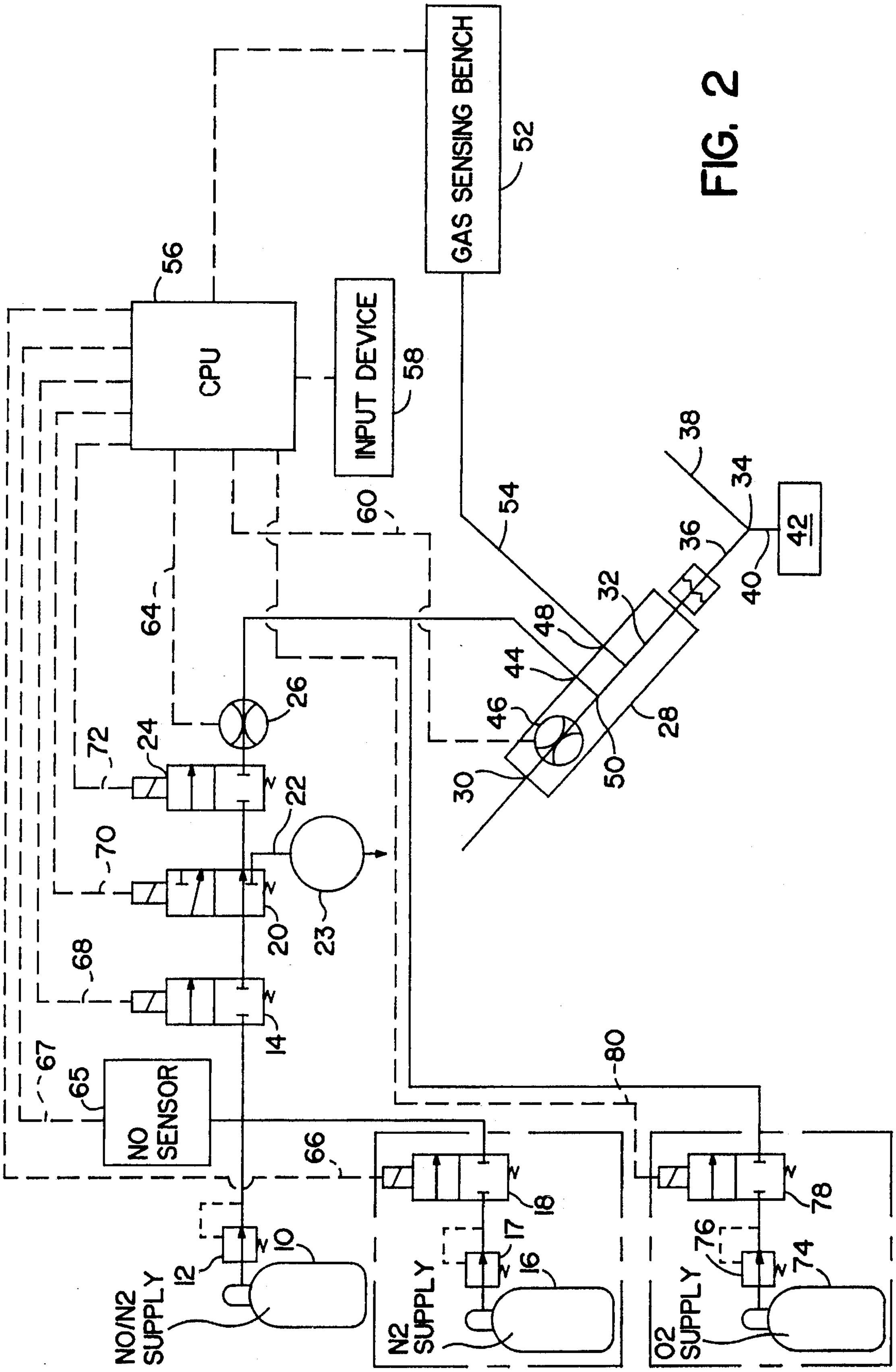

GAS SENSING BENCH
52
CPU
56
INPUT DEVICE
58
60
64
54
38
34
36
42
40
32
48
44
46
26
24
72
22
70
20
23
68
14
28
50
30
67
65
NO SENSOR
66
80
18
78
10
12
17
16
76
74
NO/N2 SUPPLY
N2 SUPPLY
O2 SUPPLY

FIG. 2

NITRIC OXIDE DELIVERY SYSTEM

BACKGROUND OF THE INVENTION

The administration of inhaled nitric oxide (NO) to patients is currently being investigated for its therapeutic effect. The use of NO has a vasodilatory effect on such patients and is particularly of importance in the case of newborns having persistent pulmonary hypertension. In such cases, the administration of NO has significantly increased the oxygen saturation in such infants.

The function of the administration of NO has been fairly widely published and typical articles appeared in The Lancet, Vol. 340, October 1992 at pages 818–820 entitled "Inhaled Nitric Oxide in Persistent Pulmonary Hypertension of the Newborn" and "Low-dose Inhalational Nitric Oxide in Persistent Pulmonary Hypertension of the Newborn" and in Anesthesiology, Vol. 78, pgs. 413–416 (1993), entitled "Inhaled NO—the past, the present and the future".

The actual administration of NO is generally carried out by its introduction into the patient as a gas along with other normal inhalation gases given to breathe the patient. Such commercially available supplies are provided in cylinders under pressure and may be at pressures of about 2000 psi and consist of a mixture of NO in nitrogen with a concentration of NO of between about 800–2000 ppm. As such, therefore, some means must be used to reduce the pressure of the supply to acceptable levels for a patient and also to very precisely meter the amount of the NO and nitrogen mixture so that the desired concentration of NO is actually administered to the patient. Such administration must also be added in sympathy with the respiration pattern of the patient.

The concentration administered to a patient will vary according to the patient and the need for the therapy but will generally include concentrations at or lower than 150 ppm. There is, of course, a need for that concentration to be precisely metered to the patient since an excess of NO can be harmful to the patient. In addition, the administration must be efficient in a timely manner in that NO is oxidized in the presence of oxygen to nitrogen dioxide and which is a toxic compound. Therefore, care in its administration is paramount.

Current known methods of such administration, therefore have been limited somewhat to clinical situations where attending personnel are qualified from a technical sense to control the mixing and administration of the NO to a patient. Such methods have included the use of a forced ventilation device, such as a mechanical ventilator where a varying flow os breathing gas is delivered to the patient as well as gas blenders or proportioners that supply a continuous flow of the breathing gas to the patient to which NO has been added.

In the former case, the use of a ventilator is constrained in that the user must know the precise flow from the ventilator and then the amount of NO to be added is determined on a case-to-case and moment-to-moment basis. Furthermore, the flow profile in forced ventilation varies continuously thereby making it impossible to track the flow manually. In the use of the latter gas blenders, the introduction of the NO containing nitrogen has been accomplished through the use of hand adjustment of the gas proportioner in accordance with a monitor that reads the concentration of NO being administered to the patient. Thus the actual concentration is continuously being adjusted by the user in accordance with the ongoing conditions of the apparatus providing the breathing mixture.

While such modes of providing a known concentration of NO to the patient may be acceptable from a closely controlled and monitored clinical setting, it is advantageous to have a system that could be used with various means of providing the breathing gas, whether by mechanical means such as a ventilator, or by the use of a gas proportioner and which could automatically adjust for that particular equipment and assure the user that the desired, proper concentration of NO is being administered to the patient.

SUMMARY OF THE INVENTION

In accordance with the present invention, there is provided a nitric oxide delivery system that is useable with various means of administering the NO, including the use of any mechanically assisted ventilation and ventilatory pattern, such as a ventilator or with spontaneous ventilation where the NO is introduced by means of a gas proportioning device that provides a continuous flow to the patient. The invention includes a flow transducer that senses the flow of gas from the gas delivery system and uses that information with a selective algorithm to provide an operator selectable concentration of NO to the patient. As used herein, the term gas delivery system is intended to include various types of gas proportioning devices, gas mixers and various types of mechanical ventilators used to provide breathing gas to a patient and may include an anesthesia machine, or manual bag, used with a patient undergoing an operation and which has a fresh gas supply.

In the preferred embodiment, a CPU obtains information from the flow transducer and from an input device that allows the user to select the desired concentration of NO to be delivered to the patient and calculates the flow of NO/nitrogen to obtain that selected concentration. It will be noted, however, that while a CPU is preferred, the signal processing needed by this system can readily be accomplished through the use of alternate technologies, such as analog or digital circuitry, fluidic circuits, optical means or mechanical components. The term "signal processing means" is intended to encompass the variety of ways that may be utilized to carry out the various signal processing functions to operate the subject NO delivery system.

Accordingly, the present system can be used with precision with various gas delivery systems, including ventilators of different manufacturers operating with diverse ventilatory patterns without the need to calculate output from the ventilator, to interrogate the gas delivery means, or to regulate the concentration manually. The user is thus free to concentrate on other procedures that will improve the patient.

By use of the CPU, various algorithms may be stored and used as appropriate. For example, there may be one algorithm that is used to obtain a steady concentration of NO in a spontaneous or continuous flow situation such as when a gas proportioner of gas blender is used. A differing use of that same algorithm may be used to achieve an instantaneous change in the NO/nitrogen supply flow to maintain the desired flow to the patient or, that same algorithm may be used to calculate a breath-by-breath flow of NO/nitrogen such that the flow from the gas delivery system may be determined and used to adjust the NO/nitrogen flow to maintain the desired NO concentration to the patient in the next breath delivered to the patient. In any manner, the CPU takes over the manual setting of any valves and established the concentration of NO to the patient as set or selected by the user.

Another use of the preferred signal processor, the CPU, is to supervise the safe operation of the NO delivery system by providing alarm functions and other functions to protect the patient in the event of faults in the delivery of NO.

As an alternate embodiment, a further means is included that adjusts the O2 concentration to the patient to compensate for the diminution of O2 to the patient as the patient inspiratory gas is loaded with NO/nitrogen to achieve a specified concentration of NO in the patients inspired gases. As a still further embodiment, a purge system is included that is activated to purge the various components and to fill the system with a gas having a known nitric oxide concentration from the supply.

The system also includes various controls, alarms and safety devices to prevent excess concentrations of NO_2 in the administration of NO to the patient, including means to shut down the NO system or to reduce the NO concentration to the patient to a safer level. The NO delivery system may thus provide an alarm or other appropriate action in the event of an increase in the NO level beyond a predetermined level, a decrease in O2 below a predetermined level and/or an increase of NO2 above a predetermined level. Depending on the severity of the alarm condition, an alarm may sound or the entire system may be controlled to alleviate the unsafe condition sensed.

These and other objects, features and advantages of the present invention will be more apparent from the detailed description of the preferred embodiment set forth below, taken in conjunction with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is a schematic view, partially in block diagram form, of apparatus in accordance with an embodiment of the present invention.

FIG. **2** is a schematic view, partially in block diagram from, of apparatus in accordance with another embodiment of the present invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Turning first to FIG. **1**, there is shown a schematic view, partially in block diagram form, showing an apparatus constructed in accordance with the present invention. In the FIG. **1**, a supply of nitric oxide is provided in the form of a cylinder **10** of gas. That gas is preferably nitric oxide mixed with nitrogen and is a commercially available mixture. Although the preferred embodiment utilizes the present commercial NO/nitrogen mixture, it is obvious that the NO may be introduced to the patient via some other gas, preferably an inert gas. Generally, of course, the cylinder **10** of nitric oxide is delivered pressurized and a typical pressure is on the order of about 2000 psi with a concentration of nitric oxide in the order of about 1000 ppm. Alternatively, the NO/nitrogen gas may be available in a central supply within a hospital and be available through the normal hospital piping system to various locations such as operating rooms. In such case, the pressure may already be reduced to a relatively lower amount that the cylinder pressures.

A pressure regulator **12** is used, therefore, to reduce the pressure of the gas in cylinder **10** down to acceptable levels for operation of the system, and again, typically, the regulator **12** reduces the pressure to about 40 psi or lower. An on-off shutoff valve **14** receives the reduced pressure gas from regulator **12** through a suitable conduit and is preferably solenoid operated. The use and purpose of the shutoff valve **14** will later be explained in conjunction with the operation of the nitric oxide delivery system.

A separate supply of pure nitrogen may be employed and, again, generally is provided by a cylinder **16** of nitrogen although pipeline nitrogen is available in numerous hospitals. The pressure of the nitrogen within cylinder **16** is reduced to the desired system level by means of regulator **17** and the nitrogen thereafter supplied via a conduit to a proportional control valve **18** that is controlled in a manner to be described. Suffice at this point is to state that the proportional control valve **18** provides a predetermined flow of nitrogen through a suitable conduit into the conduit to be mixed with the NO/nitrogen gas from cylinder **10** and which then enters the shutoff valve **14**.

The purpose of the additional supply of nitrogen is to dilute, if necessary, the concentration of nitric oxide in the supply to the shutoff valve **14** to a desired amount. For example, the cylinder **10** may be supplying a concentration of nitric oxide that is too high for the particular flows in the system and therefore the concentration may be reduced to a more desirable level. If, of course, the supply of nitric oxide from cylinder **10** is suitable for the particular application, the addition of supplemental nitrogen is unnecessary.

Further downstream in the conduit carrying the NO/nitrogen stream is a purge valve **20** and which may be a solenoid operated valve that diverts the stream of NO/nitrogen from shutoff valve **14** to a sidestream **22** where the mixture is removed from the environment by means of a hospital evacuation or other system to remove such gases. Such system may, of course, have various treatment means such as a NO2 and NO scrubber **23** if required in a particular hospital.

Again, the control of the purge valve **20** and its use will be later explained in connection with the overall operation of the nitric oxide delivery system, and which is optional.

A further proportional control valve **24** is positioned with suitable conduit to receive the NO/nitrogen gas from the purge valve **20**. Typical of such proportional control valves for both the proportional control valve **18** in the nitrogen supply system and the proportional control valve **24** in the NO/nitrogen stream may be obtained commercially from various companies, including MKS Instruments, Inc. of Andover, Mass. and which provide electronic control of gases. As may be seen, alternately, the valve may be a digital controlled valve rather that analog and which is controlled by timing its on/off cycles to effect the desired flow through the proportional control of flow therethrough. Combination of several valves used singly or in combination can be used to extend the delivery range.

A flow sensor **26** is located in the downstream conduit from proportional control valve **24** and senses the flow from such valve. Typically, in view of the values of flow at this point in the nitric oxide delivery system, the flow transducer may be of a technology such as the thermal mass flowmeter available from MKS Instruments, Inc. or may be of other technology of other suppliers.

A delivery adaptor **28** receives the NO/nitrogen gas via a suitable conduit for introduction into a further gas stream from the gas delivery system (not shown).

Delivery adaptor **28** is preferably a one piece reusable device and which has an inlet **30** which receives the gas delivered from the gas delivery system. As indicated, that gas delivery system may be a mechanical means providing a varying flow such as a ventilator, may be gas continuously supplied by a gas proportioning device for spontaneous ventilation or may be gases supplied to a bag for manual

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.

WHAT WILL YOU BUILD? | **sales@docketalarm.com** | **1-866-77-FASTCASE**

fastcase®
Smarter legal research.