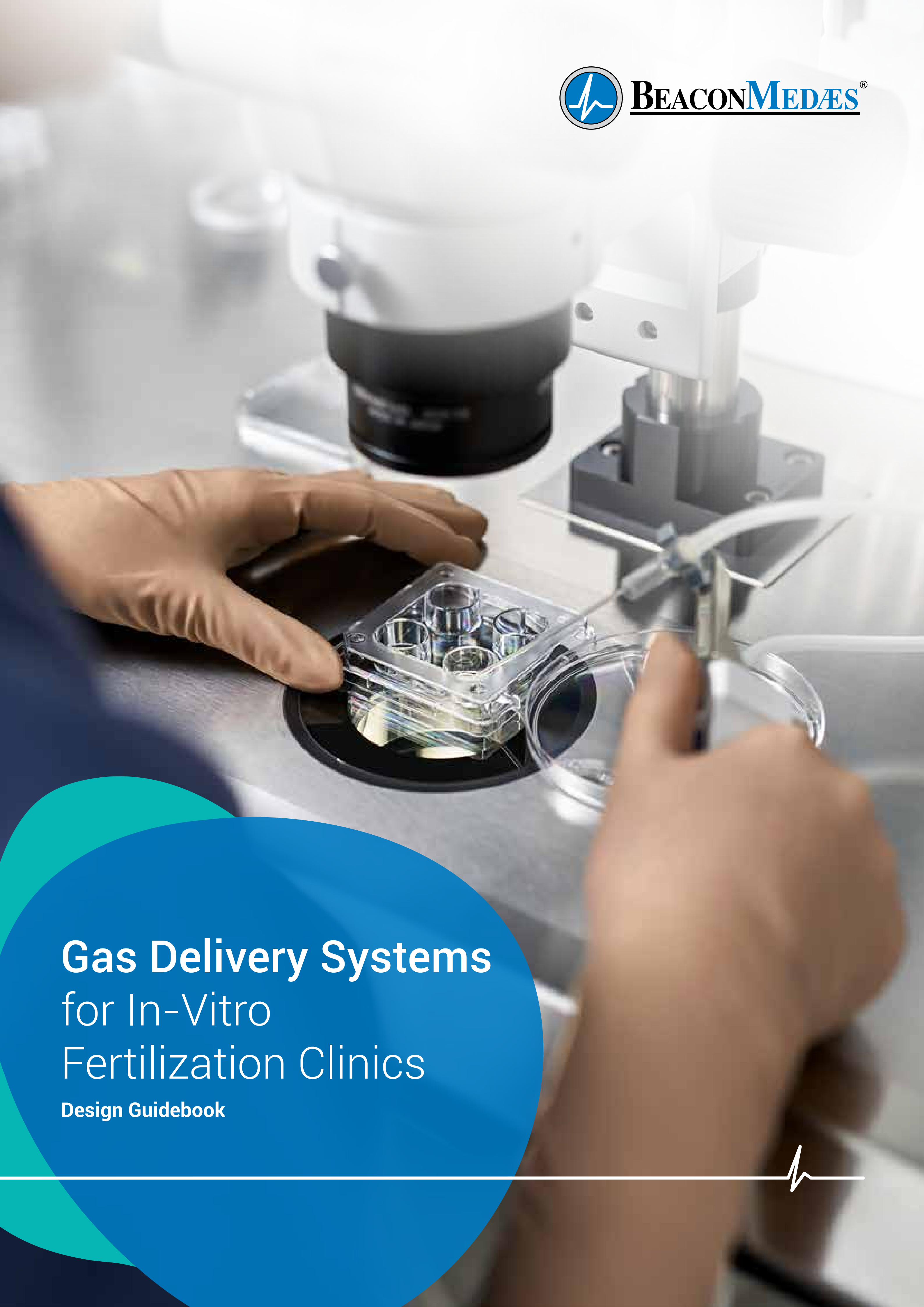
BeaconMedæs



Gas Delivery Systems for In-Vitro Fertilization Clinics

Design Guidebook

Contents

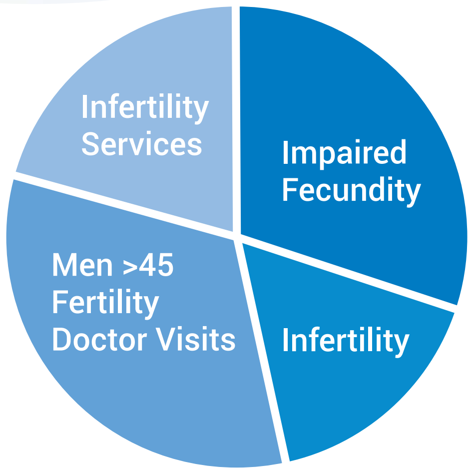
Infertility, a common problem

Infertility, a condition characterized by the inability to become pregnant despite having carefully timed, unprotected sex for a year, is experienced by roughly 1 in 5 (19%) of married women ages 15-49 in the United States, according to the CDC's National Survey of Family Growth with data for 2015-2019. Both men and women contribute to the couple's infertility.

For a pregnancy to occur, ovulation and fertilization need to work properly, according to Mayo Clinic. Many factors contribute to infertility in both men and women. Infertility problems can exist from birth (congenital) or can occur when something goes wrong. In general:

- 1/3 of cases, the cause of infertility involves only the male
- 1/3 of cases, the cause of infertility involves only the female
- 1/3 of cases, the cause of infertility involves both the male and female, or no cause can be identified

Information compiled from Mayo Clinic.



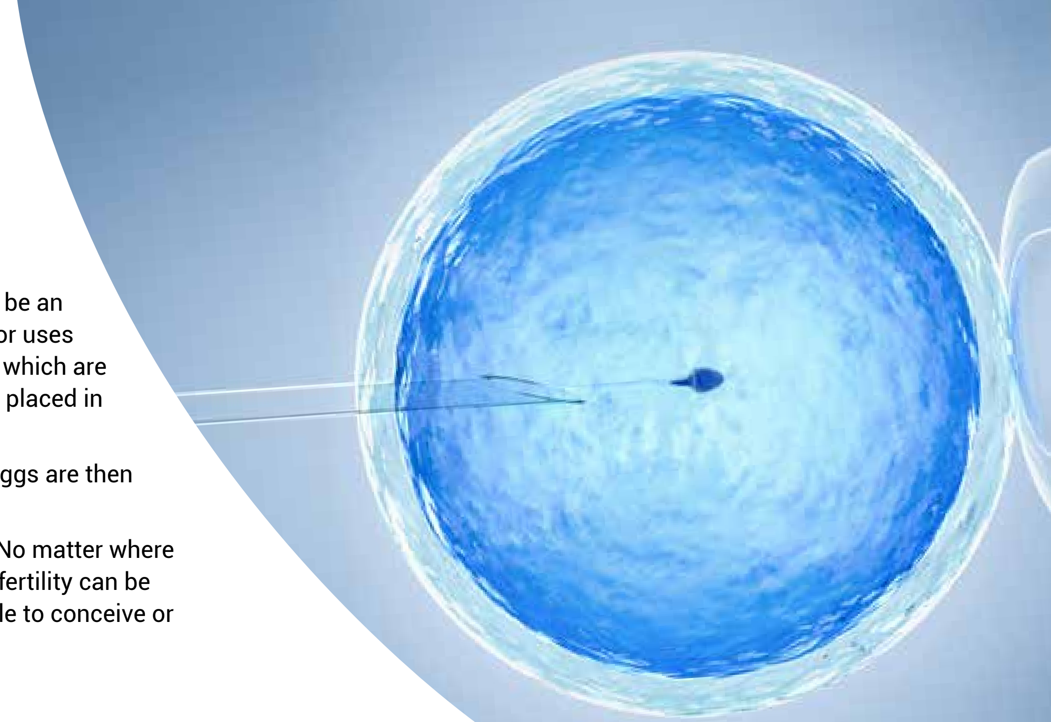
Source of data :

Centers for Disease Control and Prevention and Cleveland Clinic

Scope of infertility in the USA

- 13.8% of women ages 15-49 (having 0 births, all marital statuses) live with the impaired ability to get pregnant or carry a baby to term (impaired fecundity)
- 19.4% of married women ages 15-49 (having 0 births) are infertile
- 12.2% of women ages 15-49 have used infertility services
- According to the Cleveland Clinic, infertility affects one in every six couples trying to conceive. In roughly half of these cases of infertility, a male factor is a major or contributing cause. This means about 10% of males in the USA who are attempting to conceive suffer from infertility.

Data from 2015-2019



Why IVF

When a man or a woman is affected by infertility, In-Vitro Fertilization (IVF) may be an option for conceiving. With IVF, the doctor uses a needle to remove eggs from the ovary, which are combined with sperm in a petri dish and placed in an incubator, according to Mayo Clinic.

When fertilization occurs, the fertilized eggs are then transferred to the uterus.

As we age, the infertility rate increases. No matter where the problem occurs, the heartbreak of infertility can be devastating. Some couples are never able to conceive or carry a pregnancy to term.

Our role as gas delivery system manufacturers

As gas delivery system manufacturers, we at BeaconMedaes have a complicated task ahead of us. Our task is to provide a reliable gas distribution system that performs to expectations and is simple to operate. For the gas distribution system, we must:

- Supply very high quality gas molecules to keep harmful contaminants away from the embryos
- Provide uninterrupted supply of gas molecules to the incubators
- Provide point-of-use controls so pressure and flow can be adjusted for present and future technology
- Safely supply liquid nitrogen in the most suitable way to reduce wasted molecules while keeping the freezers from running empty
- Provide warning signals allowing for enough time to replenish the gas supply or notify personnel should the gas delivery system fail

ICSI

There are several IVF methods used in reproductive medicine. The information contained in this handbook applies to the Intracytoplasmic Sperm Injection (ICSI) method.

Medical gases

This guidebook focuses exclusively on IVF gases and on liquid nitrogen distribution systems. IVF clinics may require medical gases. We recommend you consult the "Medical Gas Design Guide" by BeaconMedaes on how to design medical gas delivery systems.

Safety first

The IVF gas delivery system designs proposed in this guidebook have taken into account the required safety recommendations.

About this handbook

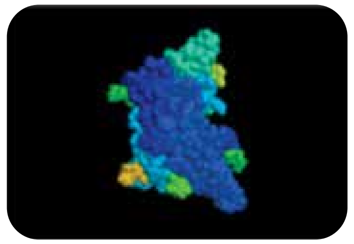
This guidebook focuses on the delivery systems for fluids most engineers, contractors, and end users struggle with; the IVF gases and liquid nitrogen.

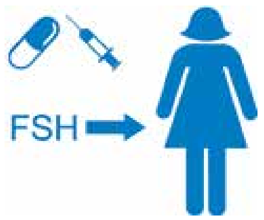
This guidebook contains flow diagrams, equipment model numbers and recommendations based on one specific way of designing gas delivery systems for IVF gases and liquid nitrogen. Keep in mind, the end user is likely to have some preferences on the design based on previous experience.

Unlike NFPA 99, which guides the design of medical gas delivery systems, gas delivery systems for IVF gases and liquid nitrogen are not guided by any specific standards or codes other than the ones applying to safety. Therefore, the final design may end up being noticeably different than what is demonstrated in this guide.

Our guidebook is not in any way intended to substitute for a properly qualified engineer. The intent of BeaconMedaes is that this guidebook should only be used as one tool by properly qualified engineers who understand its applicability and limitations.

In-Vitro Fertilization overview
Intracytoplasmic sperm injection



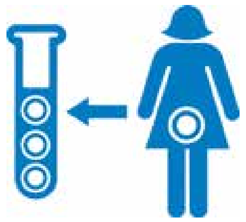


A Egg harvesting

- Daily dose of hormones over two weeks
- Goal: Stimulate the ovaries to produce eggs
- Monitored by an endocrinologist

Hormone given

- Primarily follicle-stimulating hormone (FSH)
- Synergizes with luteinizing hormone (LH)

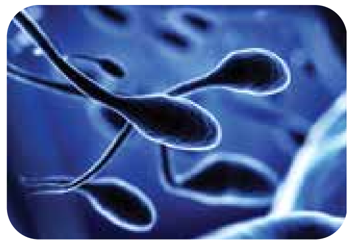


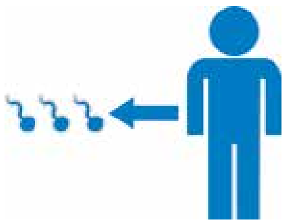
B Egg retrieval

- Aspiration of eggs under sedation
- Patient recovery time: Two hours
- 1-12 eggs are collected

Gases required for patient care:

- Medical oxygen
- Medical air
- Medical nitrous oxide

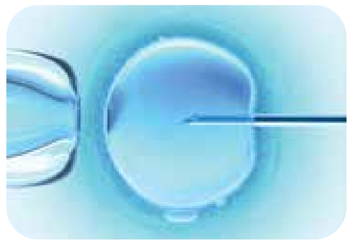




C Preparation of sperm cells

(Sperm selection)

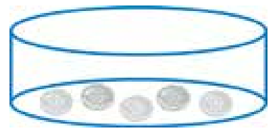
- Only mobile sperm cells are selected



D Insemination (ICSI)

(Intracytoplasmic sperm injection)

- Insemination by an embryologist
- Microinjection of each egg by one sperm cell
- 1 To 3 eggs are fertilized

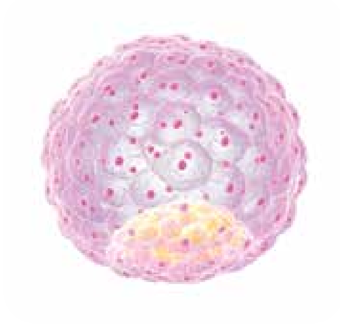


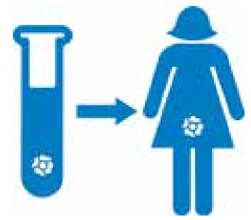
E Incubation period

- Incubation period lasts 2 to 5 days
- 65% of the eggs will be fertilized
- This time is required for the eggs to become embryos before implantation in the uterus

Gases required for cell culture:

- Carbon dioxide
- Nitrogen
- Gas mixture (aka blood gas)



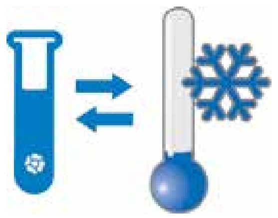


F Embryo transfer

- 1 to 3 embryos (blastocysts) are selected
- Selected embryos are placed in a thin catheter
- The catheter is inserted inside the uterus
- Blastocysts are released into the uterus
- Procedure performed by a gynecologist

Gases required for patient care:

- Medical oxygen
- Medical air
- Medical nitrous oxide



G Cryopreservation (Vitrification)

- Embryos not used are frozen in liquid nitrogen
- Embryos are labeled and stored in the embryo bank
- These embryos can be used for future cycles if pregnancy is not achieved, which simplifies the process and reduces costs

Fluids required for cryopreservation:

- Liquid nitrogen

Equipment commonly using gases in an IVF clinic

Carbon dioxide or trigas incubator

Purpose

In IVF, an incubator is a device used to grow and maintain cell cultures. The incubator maintains optimal temperature, humidity, and other conditions such as the carbon dioxide and oxygen level content of the atmosphere inside.

More specifically, the carbon dioxide reacts with water molecules (H_2O) in the medium (liquid containing blastocysts and embryos) to generate HCO_3- which acts as a buffering system for the cells in the medium. The optimum concentration of CO_2 for pH maintenance is 5%.

The role of oxygen is to recreate - in the medium - the normal and optimal oxygen partial pressure normally found in human blood. The amount of oxygen in the medium is dependent on how much carbon dioxide is in the incubator. The level will vary between 5% and 10%.

The role of nitrogen is passive. It is the balance gas in the oxygen-carbon dioxide tri-gas mixture.

Information compiled from Thermo Fisher Scientific.

Gas used

Carbon Dioxide, Nitrogen, Tri-gas

Note to designer

Not all incubators are supplied solely with carbon dioxide and nitrogen. In fact, several incubators must be supplied with tri-gas. It is not unusual for an owner to opt for an Air-CO_2 mixer as opposed to using bottled tri-gas.

Incubator

Photograph used by permission from Thermo Fisher Scientific.

IVF workstation

Purpose

IVF workstations are specifically designed for aseptic handling of sperm cells, oocytes, and embryos to minimize microbial contamination. Several IVF workstations are equipped with a heating system with a maximum variation of ±0.2ºC of the heated area. Proper lighting is crucial, so all IVF workstations also include an integrated light base. Newer versions of IVF workstations include a built-in stereomicroscope fitting, a transmitted light source, and a table plate which is heated either through electrical heating or water circulation heating. Below are some features and benefits of IVF workstations:

1. Minimal noise level (less than 55 dB)
2. A built-in gassing and humidifying system controls the pH and osmolality
3. Flushing CO_2-gas mixture maintains correct pH
4. Prevents frequent openings of CO_2-incubator
5. Temperature is controlled with a built-in heated area in the table plate
6. Maximum work area in well-lit laminar flow cabinet, flushed with a vertical flow of HEPA filtered air
7. Microscopes already in use and microscopes purchased separately can be built into the workstation

Information compiled from Ruskinn Life Sciences.

Gas used

Gas Mixture, Carbon Dioxide, and Nitrogen.

Note to designer

It is paramount to establish a list of gases for each IVF workstation as not all units require gas.

IVF workstation

Image used by permission from Ruskinn Life Sciences.

Controlled-rate freezer

Purpose

Controlled-rate freezers are used to gradually reduce the temperature of the species (embryos and sperm) in a way that allows a sufficient amount of water to leave the cell.

This instrument minimizes the lethal intracellular freezing that can occur when the species are frozen too rapidly.

Fluid used

Exclusively liquid nitrogen.

Warning to designer

Controlled-rate freezers require uninterrupted supply of liquid nitrogen during a freezing cycle.

It is highly recommended to supply liquid nitrogen using a dedicated vacuum jacketed pipe and a dedicated (separate) liquid cylinder.

Controlled rate freezer

Photograph used by permission from Thermo Fisher Scientific.

Liquid nitrogen (open flask) dewars

Purposes

Liquid nitrogen dewars have two (2) purposes:

- Transportation of species between two locations while keeping them frozen
- Short-term cryogenic preservation of species

Note: It is not unusual to see IVF clinics using dewars for long term storage of species.

Fluid used

Exclusively liquid nitrogen

Notes to designer

Most clinics keep a significantly large “fleet” of liquid nitrogen dewars. Three (3) design criteria must be kept in mind:

- Plan enough floor space for current conditions and for future expansions of the clinic
- Plan for an oxygen depletion monitor as dewars are not sealed, meaning gaseous nitrogen can escape, depleting the oxygen level in the room
- Liquid nitrogen may escape from the liquid nitrogen transfer hose and spill on the floor which can embrittle and damage the flooring material

Liquid nitrogen dewar

www.chartindustries.com

Image courtesy of Chart Industries.

Cryogenic freezers

Purpose

Cryogenic freezers are used for short, medium and long-term storage of species in liquid nitrogen.

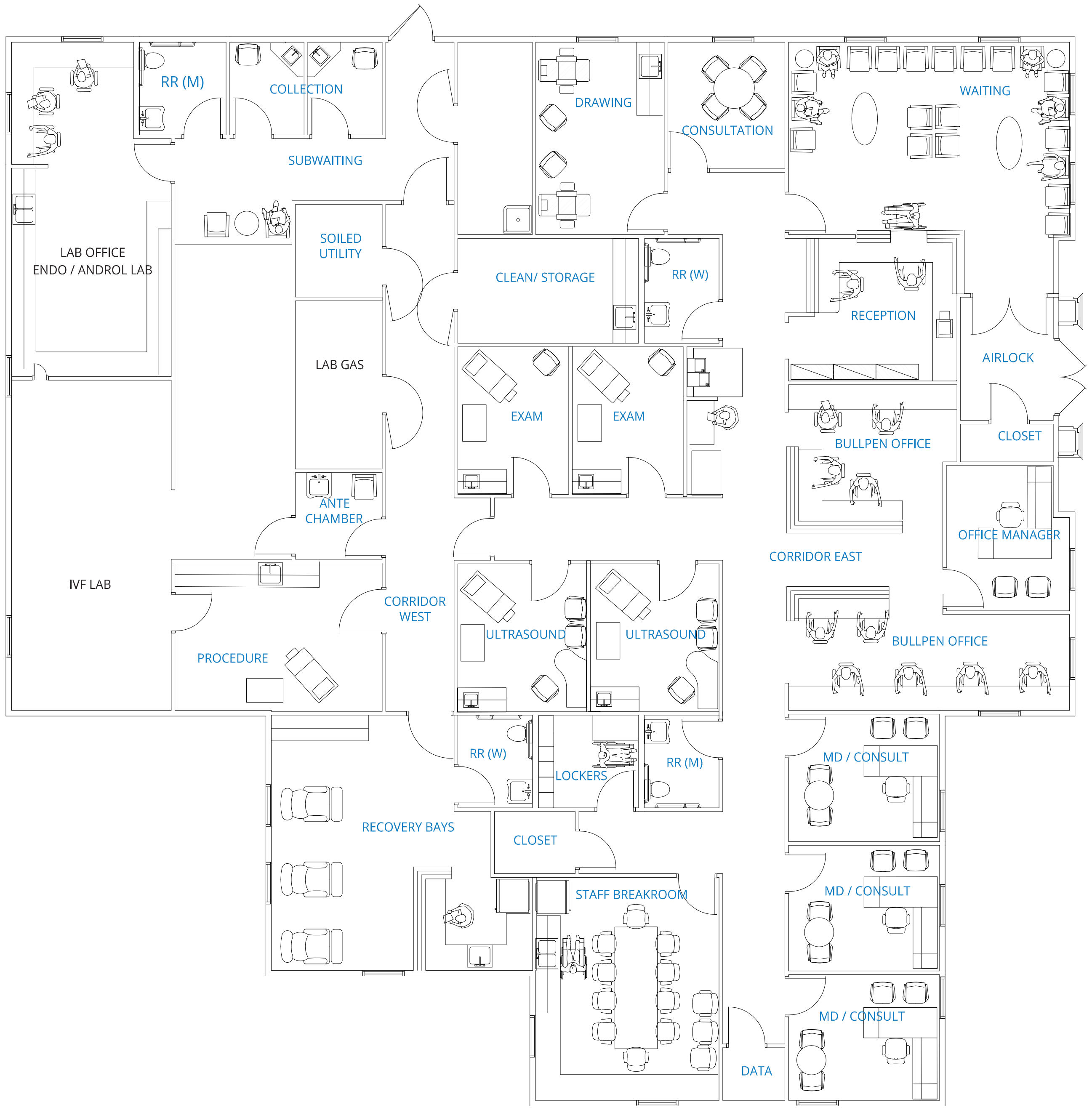
Fluid used

Exclusively liquid nitrogen.

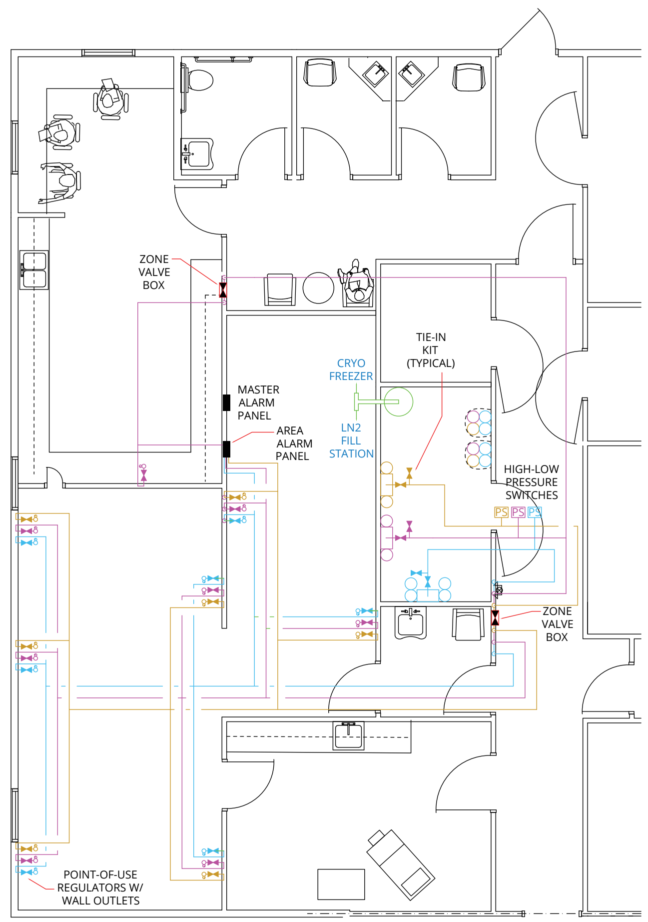
Notes to designer

Cryogenic freezers are fairly expensive and may have a large footprint. It is quite common to see IVF clinics without cryogenic freezers, especially if the clinic is in its start-up phase. BeaconMedaes recommends designing the cryogenic vacuum jacketed piping with a capped tee for future expansion.

Typical IVF clinic layout

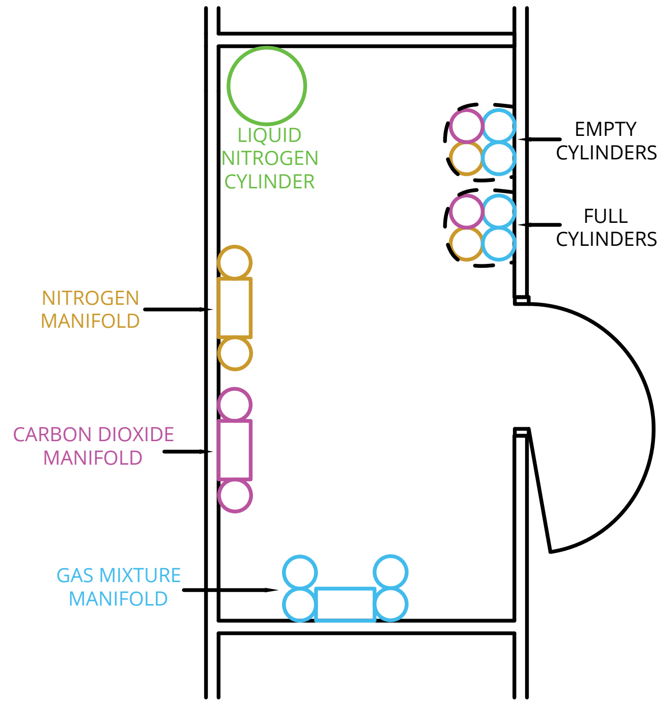


Piping schematic



The piping layout above is shown for training purposes only.

Gas tank storage (manifold room) layout



The manifold layout above is shown for training purposes only.

It's a small world

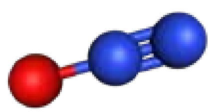
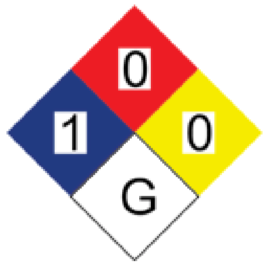
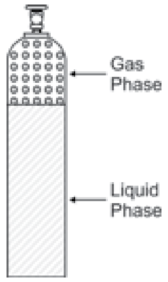
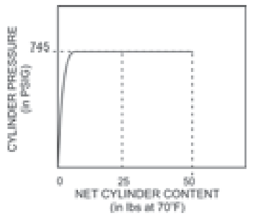
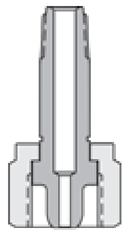
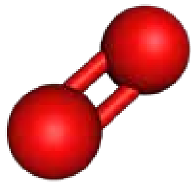
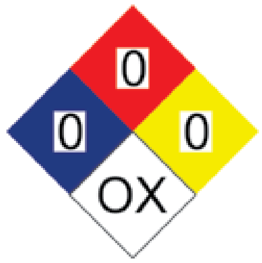
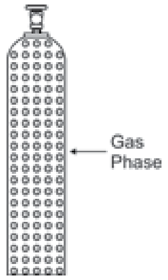
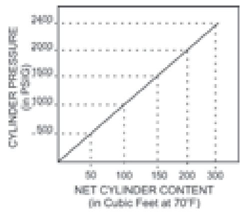
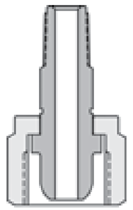
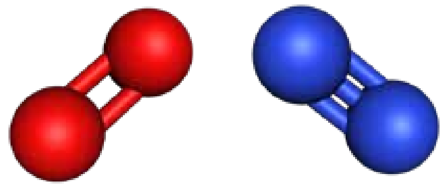
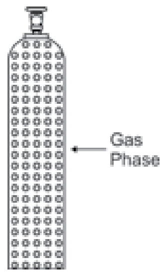
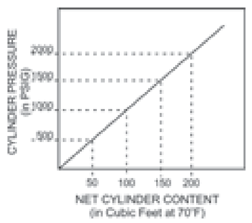
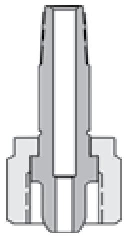
IVF clinics are small in nature but all services related to the IVF process must be present. The floor plan above shows the amenities generally found in IVF clinics: patient care area, laboratories, restrooms and offices. Offices are important to accommodate not only the administration personnel but also embryologists, endocrinologists, gynecologists and nurses.

As demonstrated on the next page, there are two (2) rooms where "IVF gases" are being piped: embryology and sometimes andrology. The area reserved for the gas tanks is generally small and located as close as possible to the embryology room.

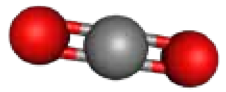
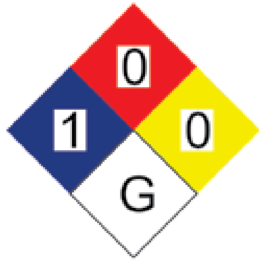
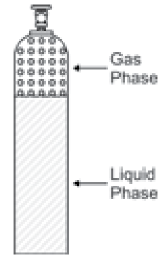
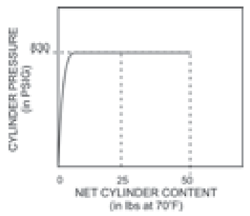
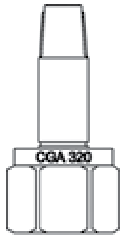
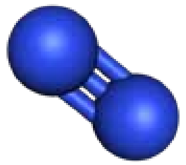
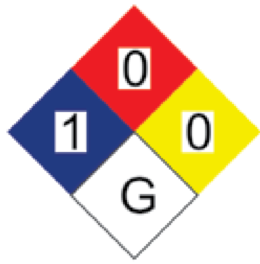
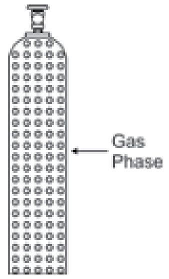
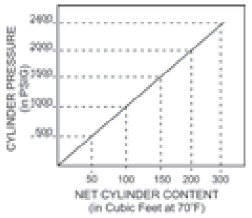
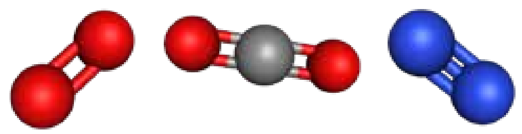
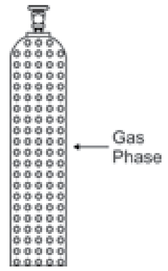
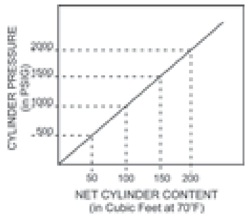
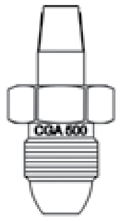
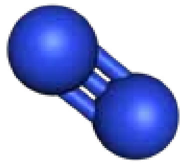
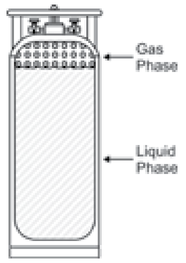
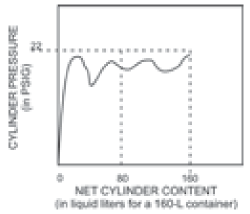
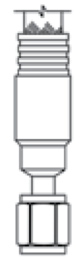
Keep it clean

An important point, the cryogenic storage room is purposely accessible only from the embryology room, where the In-Vitro Fertilization process takes place. Similarly, you can only access the embryology room from the anteroom. The cleanliness of this room is of paramount importance. Cleanliness is critical as it minimizes contamination of embryos, laboratory equipment, and chemicals.

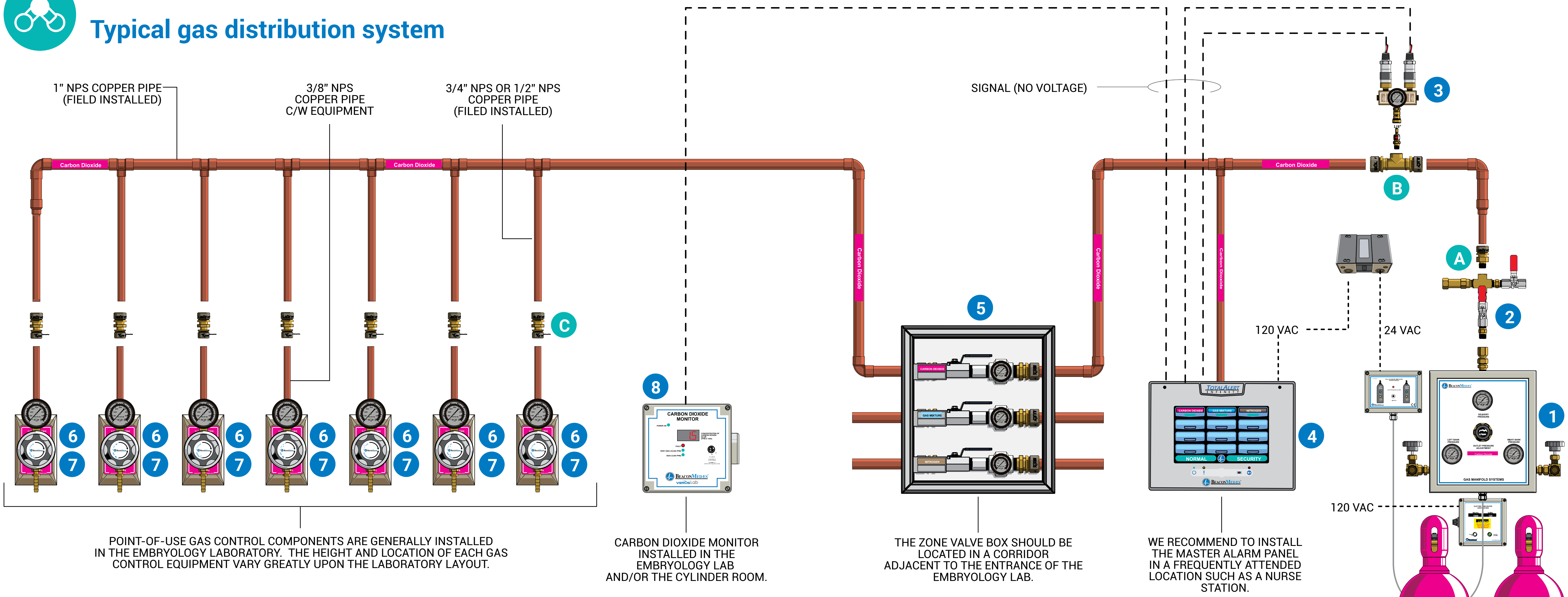
Properties of patient care gases

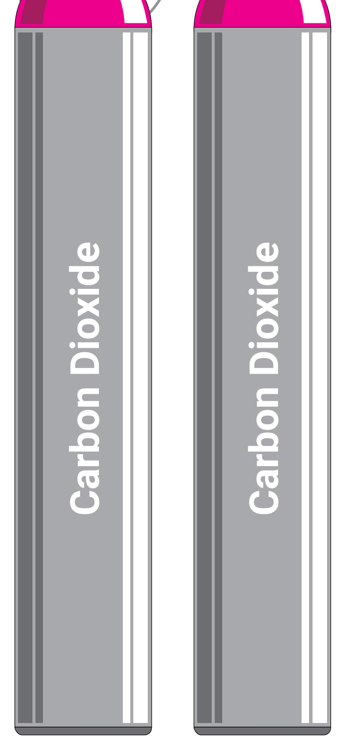
Compositions	Primary safety hazards	Molecule phases	Cylinder pressure	Cylinder connections
Nitrous oxide USP				
				 CGA 326
Oxygen USP				
				 CGA 540
Air USP				
				 CGA 346

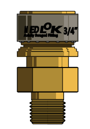
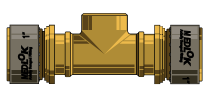
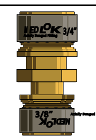
Properties of cell culture gases and liquid nitrogen for cryopreservation

Compositions	Primary safety hazards	Molecule phases	Cylinder pressure	Cylinder connections
Carbon dioxide				
	 Poison to Human at 35,000 ppm			 CGA 320
Nitrogen				
	 Nitrogen Displaces Oxygen in Air (Oxygen Depletion)			 CGA 580
Gas mixture (also known as blood gas)				
				 CGA 500 (Confirm with Gas Supplier)
Liquid nitrogen				
	 Oxygen Depletion, Cryogenic Burns, Cold Embrittlement			 CGA 295

Typical gas distribution system



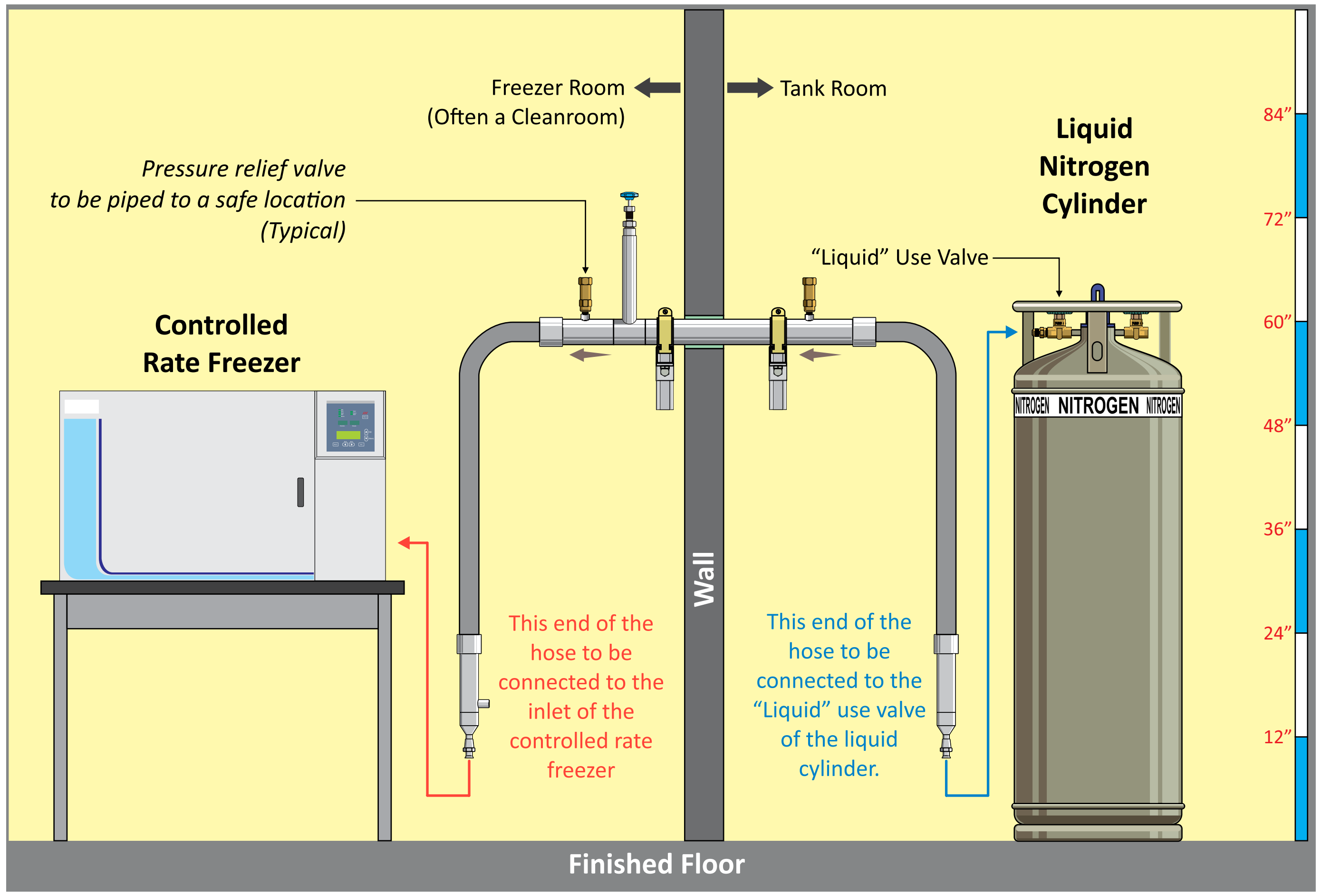


TYPICAL AXIALLY SWAGED FITTINGS[1]		
A		Male Connector 3/4" NPS (7/8" O.D.) Compression x 1/2" M.NPT
B		Female Run Tee 1" NPS (1-1/8" O.D.) Compression x 3/8" F.NPT
C		Compression Union 3/4" NPS (7/8" O.D.) Compression x 3/8" NPS (1/2" O.D.) Compression

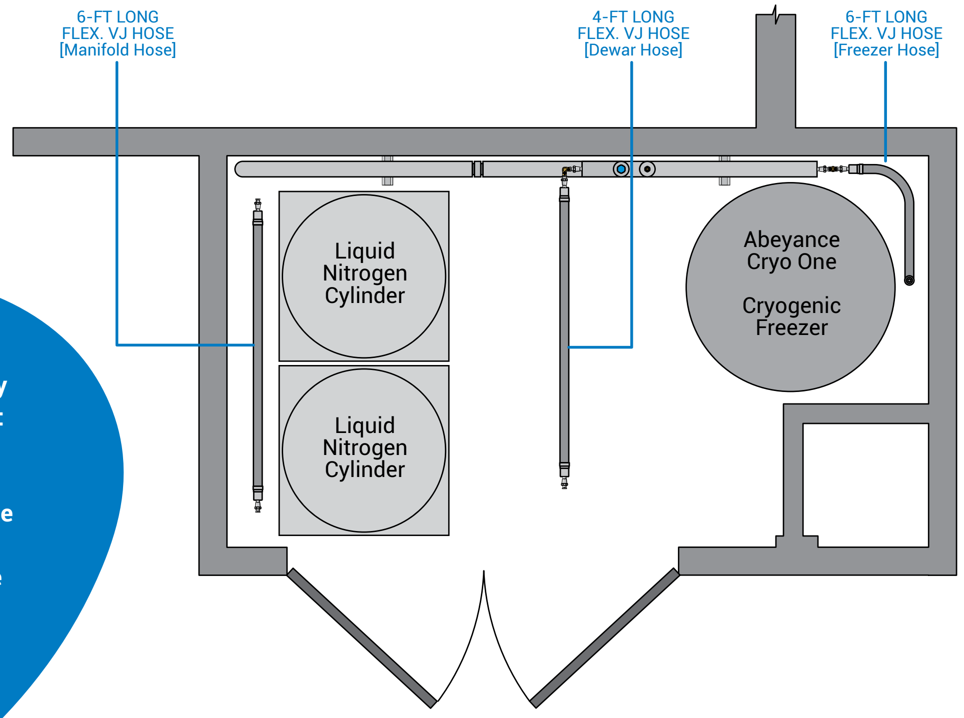
[1] We recommend to use as many axially swaged fittings as possible to connect the silver brazed copper piping to the gas equipment. This will speed up installation and minimize introduction of brazing dust to the gas equipment.

GAS EQUIPMENT SCHEDULE		
1	**AFAM1500HB Series**	Fully Automatic Switchover Manifold
2	**TIK Series**	Manifold Tie-In Kit
3	**HLPS Series**	High/Low Pressure Switch Assembly
4	**TAi Series**	TotalAlert Infinity Master Alarm Panel
5	**ZVBL Series**	Zone Valve Box for Laboratories
6	**MBB Series**	Back Entry Single-Stage Regulator
7	**WOA Series**	Wall Outlet for Analytical Applications
8	**FGM Series**	Fixed Gas Monitor

Typical liquid nitrogen piping to controlled rate freezers

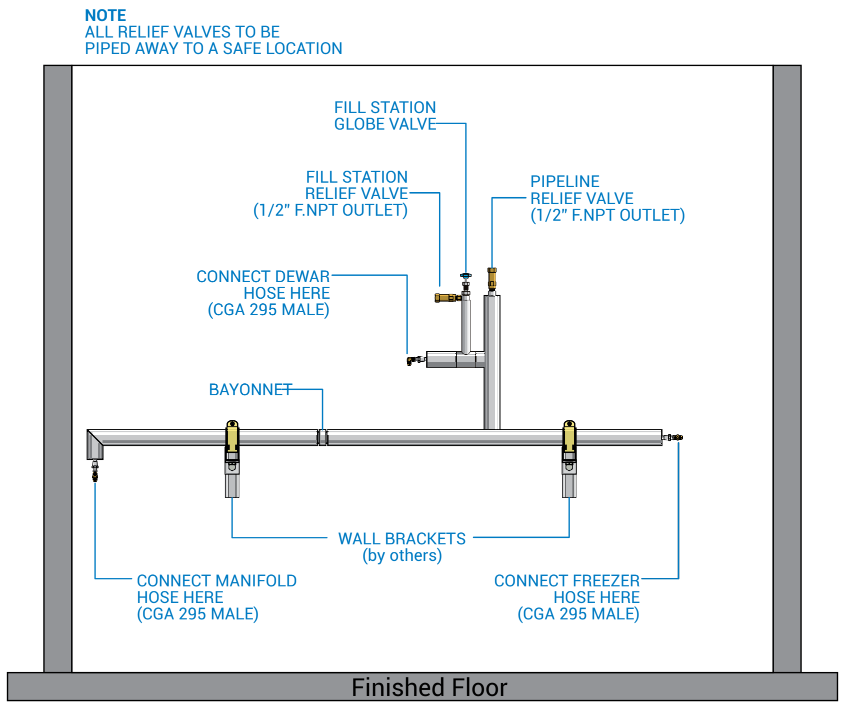


Cryogenic liquid nitrogen storage and dispense example

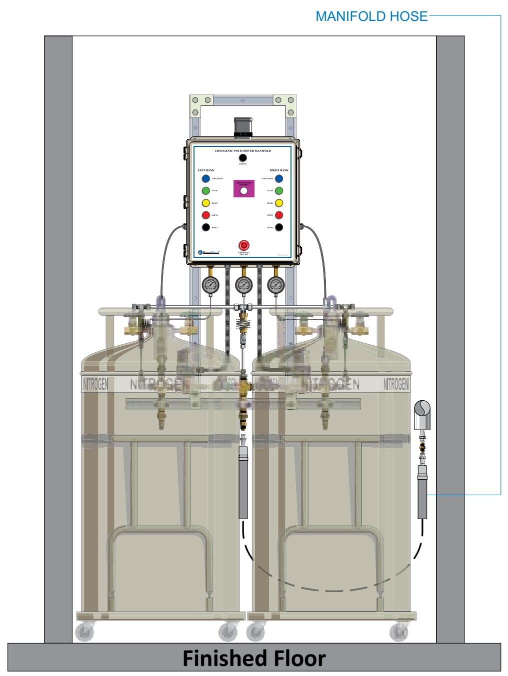


Liquid nitrogen is used primarily by three (3) types of equipment: cryogenic storage freezers, portable dewar fill stations and, in some facilities, controlled rate freezers. Shown on the right is a storage freezer and a portable dewar fill station, both located in the same room with the cryogenic manifold.

Cryogenic Room example - Top View



Cryogenic Vacuum Jacket Piping

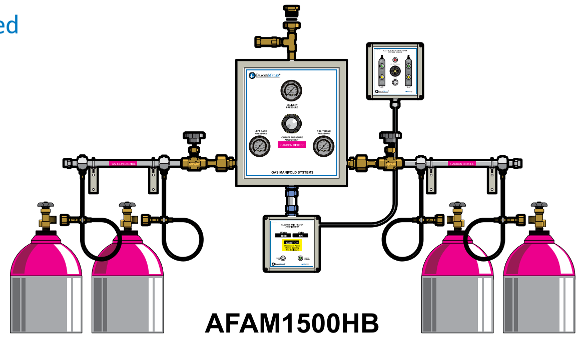


Cryogenic Manifold

General equipment specifications
Gas cylinder discharging

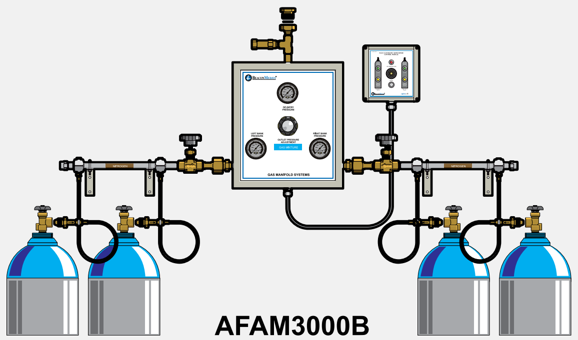
Carbon dioxide manifold (AFAM1500HB-IVF series)

Flow	500 scfh
Delivery pressure	30-125 PSI
Number of cylinders	Minimum four (4)* is recommended
Header bar specifications	Nickel plated brass, stainless steel hoses
Internal fittings and tubing material	Brass and type 316 stainless steel (copper free)
Inlet and outlet connections	Inlet: CGA 320 nut & nipple / outlet 1/2" F.NPT
Power requirement	120 VAC to power the gas heaters 120 VAC to power the manifold controller



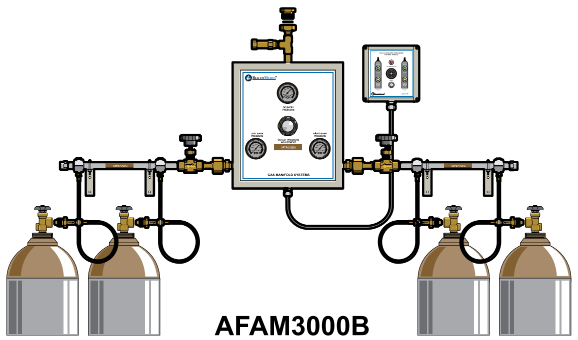
Blood gas manifold (AFAM3000B-IVF series)

Flow	Cv = 0.4
Delivery pressure	30-125 PSI
Number of cylinders	Minimum two (2)*
Header bar specifications	Nickel plated brass, stainless steel hoses
Internal fittings and tubing material	Brass and type 316 stainless steel (copper free)
Inlet and outlet connections	Inlet: CGA 500 nut & nipple / outlet 1/2" F.NPT
Power requirement	120 VAC to power the manifold controller



Nitrogen manifold (AFAM3000B-IVF series)

Flow	Cv = 0.4
Delivery pressure	30-125 PSI
Number of cylinders	Minimum four (4)*
Header bar specifications	Nickel plated brass, stainless steel hoses
Internal fittings and tubing material	Brass and type 316 stainless steel (copper free)
Inlet and outlet connection	Inlet: CGA 580 nut & nipple / outlet 1/2" F.NPT
Power requirement	120 VAC to power the manifold controller

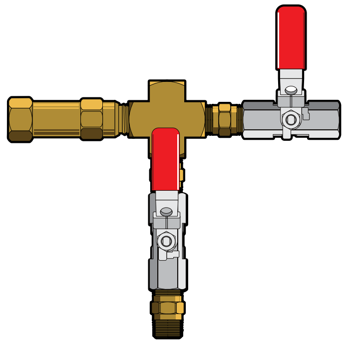


*Please refer to the Design section of this guidebook to determine the number of cylinders suitable for your application.

General equipment specifications
Pipeline accessories

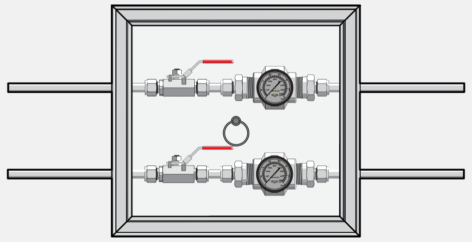
Tie-in kits (TIK series)

Inlet / outlet	1/2" M.NPT / 1/2" F.NPT
Nominal pipe size	1/2"
Standard / maximum pressure	150 PSI / 2000 PSI
Ball valve materials	Type 316 stainless steel & teflon
Standard fittings material	Brass
Optional fittings material	Type 316 stainless steel
Optional instrumentation	Pressure relief valve or pressure gauge



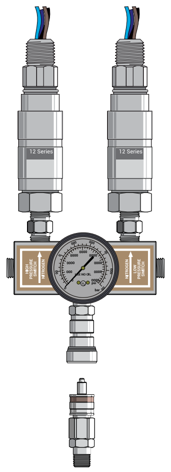
Zone valve boxes (ZVBL series)

Recommended tube/pipe size	3/4" tube or 3/4" NPS
Enclosure materials	Aluminum
Standard / maximum pressure	150 PSI / 2000 PSI
Ball valve materials	Type 316 stainless steel & Teflon
Standard fittings material	Type 316 stainless steel
Optional fittings material	Brass (available with copper tubes only)
Pressure gauge dial	2"


ZVBL Horizontal

High low pressure switch assemblies (HLPS series)

Inlet	1/4" M.NPT or 3/5" F.NPT
Pipeline-to-assembly connection	Gas indexed quick connects
Maximum working pressure	250 PSI
Pressure gauge dial	2"
Standard / optional fittings materials	Brass / type 316 stainless steel
Pressure switch ratings	NEMA 4 or NEMA 7
Optional instrumentation	Diaphragm vent valve



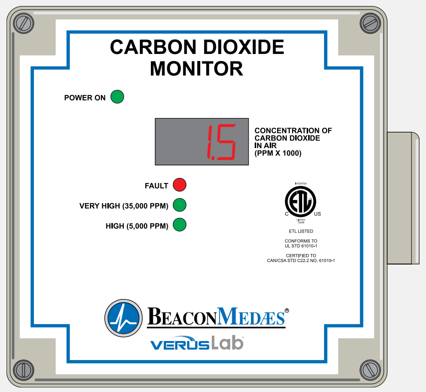
General equipment specifications
Safety and annunciation

Master / Area alarm boxes (TotalAlert Infinity™)

Possible configuration	Master or area alarm
Maximum number of inputs	Up to 64
Display and action	Touch screen
Installation	Recessed (indoor only)
Programming	Factory-programmed but can be changed in the field
Units of measure	PSI, BAR, and kPa
Power requirement	100 to 250 VAC, 50/60 Hz, 250 mA

Carbon dioxide or oxygen depletion monitor (FGM series)

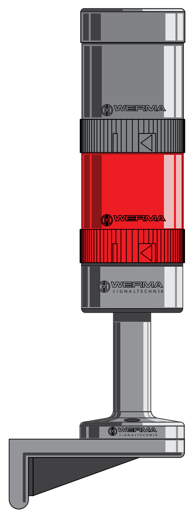
Gas detected	Carbon dioxide or Oxygen [Depletion]
Power requirement	24 to 250 VAC
Sensing technology (oxygen)	Electrochemical
Sensing technology (carbon dioxide)	Non dispersive infrared
Available output	Dry contacts and/or 4-20 mA
Sensor mounting	Inboard and/or remote
Onboard warning signal	Audible and visual alarm



Note: Carbon dioxide FGM series shown

Audio-Visual alarm (SFBH series)

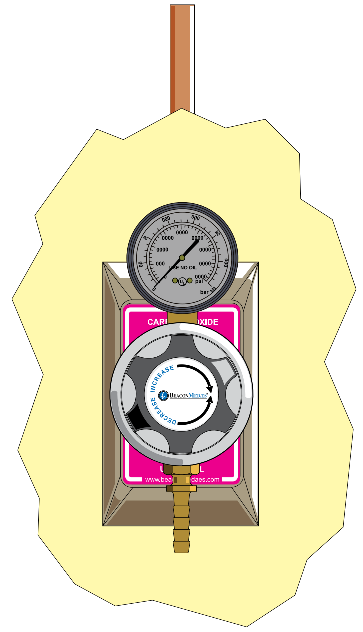
Current consumption	Less than 65 mA
Buzzer maximum volume	85 dB
Life duration	Buzzer: 500 hours - LED: 100,000 hours
Buzzer tone type	Continuous or pulse (field selectable)
Housing materials	Polycarbonate
Wiring type	AWG 18 to AWG 14
Installation	Indoor



General equipment specifications
Point-of-use control

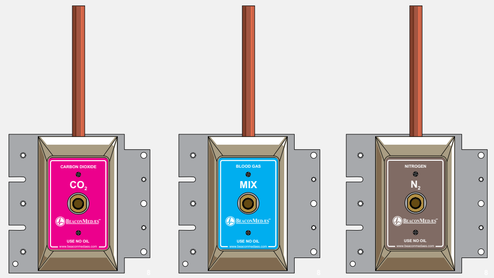
Point-of-use pressure reducing regulator (MBB series)

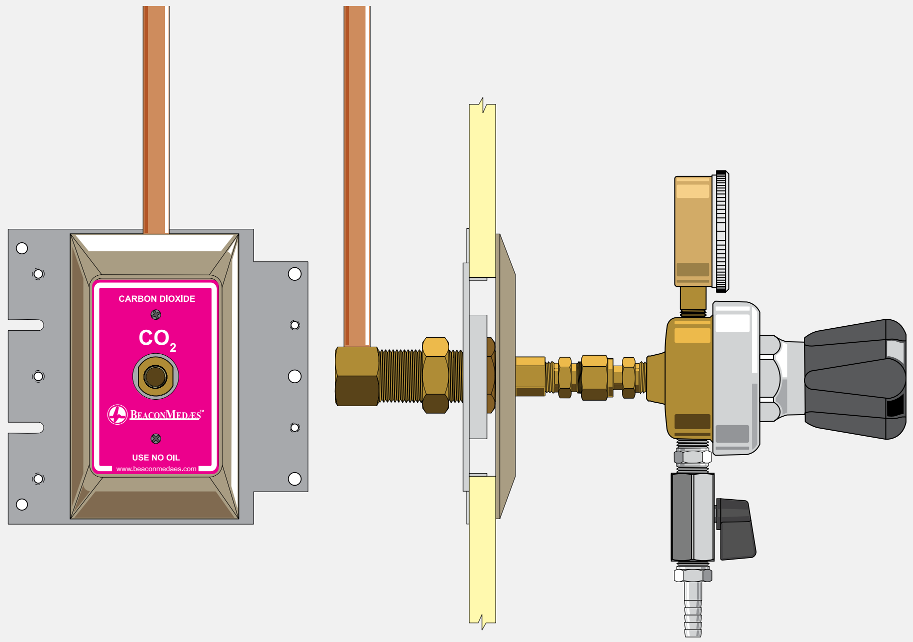
Maximum inlet pressure	200 psig
Flow coefficient	Cv = 0.57
Delivery pressure gauge	0-60 PSI
Delivery pressure range	5-50 PSI
Gauge body	Brass
Diaphragm	Stainless steel
Bonnet	Chrome-plated die cast
Knob	ABS plastic



Wall outlet for non-medical applications (WOA series)

Basis of front panel	BeaconMedaes Series B
Tube size and material	1/2" O.D. Type 316 stainless steel (copper is optional)
Back body material	Brass (stainless steel is optional)
Ball valve material	Chrome-plated brass (stainless steel is optional)
Fascia material	Lexan over vinyl (color coding is gas specific)
Fascia color code	SEFA (Scientific Equipment and Furniture Association)
Maximum wall thickness	1-1/2"
Wall outlet connection	1/4" M.NPT or 1/4" F.NPT
Maximum working pressure	200 PSI



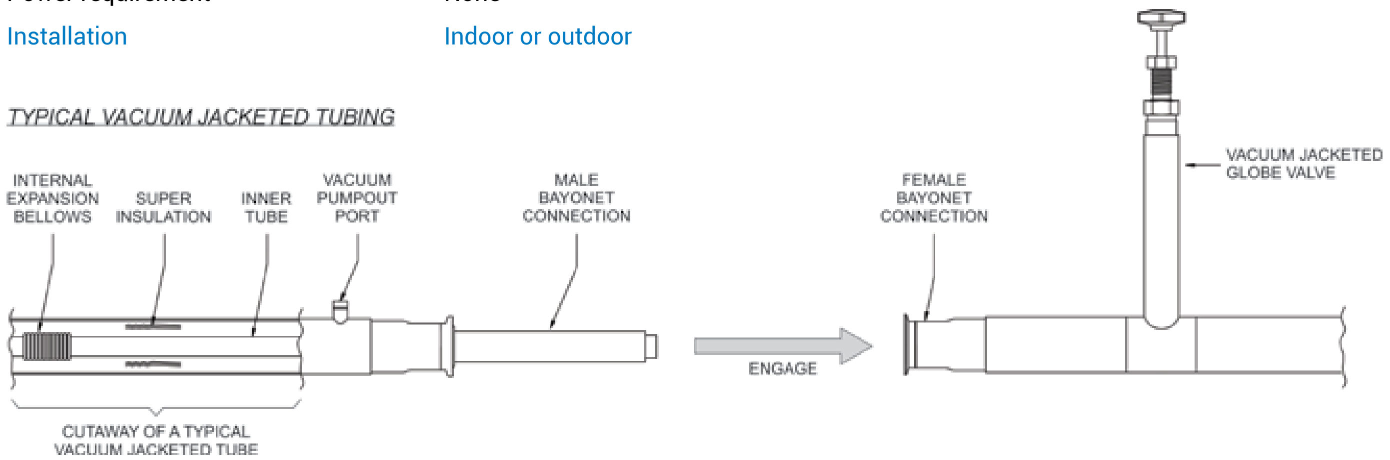


General equipment specification
Cryogenic fluid handling

Vacuum jacketed piping (VJP series)

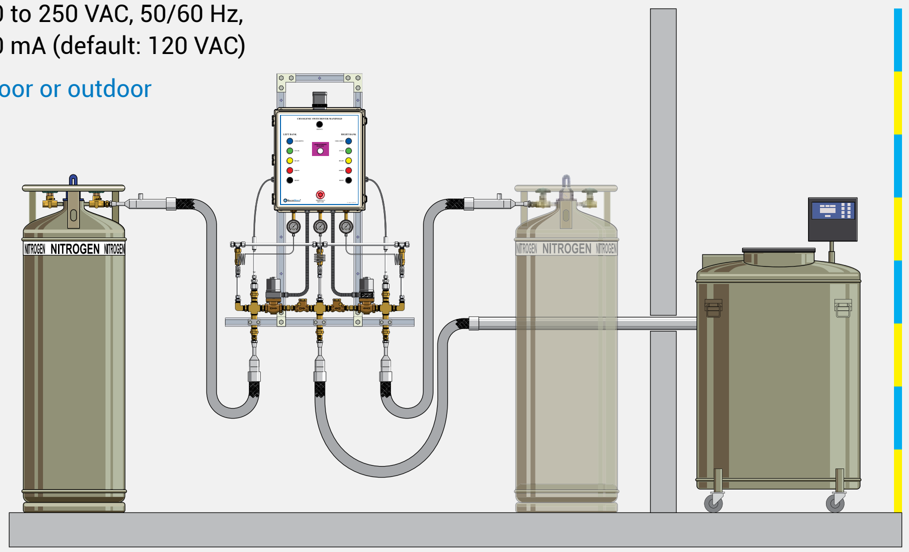
Inner conduit	1/2" NPS
Outer shell	2" NPS
Connection between spools	Male and female bayonets
Materials	Types 304 & 316 stainless steel
Vacuum rating	10^{-8} to 10^{-9} Torr
Power requirement	None
Installation	Indoor or outdoor

TYPICAL VACUUM JACKETED TUBING



Fully automatic cryogenic switchover manifold (CFAM-TX series)

Fluid delivered	Cryogenic liquid nitrogen
Preferred cryogenic fluid mode of supply	Liquid cylinders or micro-bulk
Maximum inlet pressure	50 PSI
Wetted parts materials	Brass
Enclosure material and rating	Polyester / NEMA 4X
Power requirement	100 to 250 VAC, 50/60 Hz, 250 mA (default: 120 VAC)
Installation	Indoor or outdoor



Important design criteria
cell culture gases

Why go with stainless steel tubing as opposed to copper?

There are numerous scientific studies showing copper affects embryos in different ways. In fact, the number of hits on Google for “copper toxicity on embryos” is surprisingly high. On the other hand, Google hits for “stainless steel on embryos” is almost nonexistent.

Therefore, it is understood that copper embryo-toxicity is definitely a concern whereas stainless steel embryo-toxicity is not.

The problem with copper is in several folds:

- Copper is a “flaky” metal that leaches in small quantities in the gas stream.
- Copper oxides formed from the silver brazing process are present in piping and in the gas stream in small quantities.
- Copper particles are a common contaminant in the piping network (primarily when the piping network is new) and are carried away in the gas stream up to the points of use.

How many cylinders do I need per manifold?

The number of cylinders required has a tremendous impact on the design of the gas delivery systems as well as the size of the gas cylinder room. Also, some IVF clinics use incubators for tri-gas while others use nitrogen and carbon dioxide.

The information you will collect during the discovery phase will help you determine the gases used per incubator. Below is a list of criteria impacting the manifold size for each gas:

- **The size of each incubator -** In IVF clinics, some owners may prefer to have several small incubators instead of a few larger ones. This is because each time an incubator door is open, the gas (carbon dioxide, nitrogen or tri-gas) evaporates out of the incubator and has to be replenished.
- **The number of times per day the incubator doors are opened -** The more the incubator doors are opened, the more gas is needed to replenish the incubators. Each incubator also requires a small amount of gas supply to keep the internal atmosphere within an acceptable gas concentration.
- **The number of incubators -** The more incubators in an IVF lab, the more gas is required.

The exercise of determining how much gas is needed per incubator can be done by using our calculation spreadsheet. Please contact your local BeaconMedaes representative for a copy of this spreadsheet.

Once you have determined how much gas is required by each incubator, follow these simple rules for sizing each manifold:

a. Each bank must be sized so that there is one full week of gas supply for each gas manifold header bar.

b. There has to be one week of gas supply in reserve in the cylinder room.

c. The gas supplier should be scheduled to pick up empty cylinders and drop off full ones at each visit to the IVF clinic.

What are the recommended pipeline sizes?

- A typical IVF Clinic requires - for each gas - a main conduit of 3/4" diameter and, branching off of that main conduit, BeaconMedaes suggests a 1/2" diameter conduit per drop.

What type of joints between tubes/pipes are the best?

We recommend **stainless steel tubing** (not piping).

- The best way of interconnecting stainless steel tubes together is to use the orbital welding technique.
- If the owner considers orbital welding too expensive, compression fittings may also be used.

For those who consider using copper pipes, it is recommended to:

- Follow the NFPA 99 requirements for the installation of medical copper piping.
- Make sure the installer is brazing under adequate nitrogen purge.
- It is very important to flush impurities out of the system **prior to installing** manifolds, regulators and point of use instruments.

What is the recommended gas pipeline pressure?

Many recommend the pipeline pressure should be set at 15 psi for all gases. That was true years ago when the first fertility clinics started to open around the world. However, **many techniques have evolved** and the list of equipment using any of the three (3) IVF gases has grown. These new techniques and new equipment **now require pressures different than 15 psi** (most of them greater than 15 psi). To keep up with the evolving technologies, it is recommended to set the pipeline pressure for each of the three (3) IVF gases at 100 psi. Each point of use should have a pressure reducing regulator so the pressure can be adjusted according to specific requirements. Currently, point-of-use regulators with a 5-50 psig delivery pressure range cover most pressure requirements throughout the IVF clinic.

Setting the manifold delivery pressure at 15 psi leads to the following complications:

1. All alarm set pressures in each system will need to be readjusted.
2. Some of the equipment will still run at 15 psi and new regulators and valves will be needed.
3. Should the pipeline pressure start to fall - for mechanical reasons or for other reasons - the pipeline cannot act as a "gas buffer". Therefore, when the alarm sounds for low pressure, it's too late because the gas has already run out.
4. As more equipment is added to the pipelines, the total flow of gas will increase. The higher the pipeline pressure is, the greater the flow. Conversely, a pipeline set at 15 psi has much less flow than one set at 100 psi.

Why must the gas delivery system be considered as high purity grade and not medical grade?

The success rate of IVF is not 100%. Researchers, doctors, embryologists and endocrinologists are constantly improving their techniques and seeking ways to improve the success rate. Many unsuccessful births can be linked to physiological and biological complications which are more difficult to control. **Among more controllable factors linked to the birth success rate is contamination from different sources:**

- Both **bacterial** and **fungal** contaminations are among the worst fears of embryologists.
- **Particles** of any shape, nature and quantity can harm embryos, oocytes and blastocysts. Many IVF workstations are equipped with high performance filters, and embryologists and all other IVF technicians are required to wear special gear prior to entering the embryology lab.
- **Copper** contamination is also a concern.
- **Hydrocarbons** are another undesired species in the gas stream. IVF clinics go to great lengths to eliminate any material that is not directly called for in their clinical and laboratory protocols. Embryos do not have the basic enzyme capability to remove the environmental insults (Cytochrome p450 enzyme system). The exposure to these agents also comes at the time when the embryos are doing a huge amount of genetic work for growth.

An IVF clinic is far from a standard patient care environment. That's why specifying medical manifolds are not adequate. Embryology laboratories are highly controlled environments. The requirements for higher purity is already on the rise as technology and science evolve. **The gas delivery system must not be the weakest link and it must keep up not only for today, but for tomorrow as well.** For many, **LIFE** starts in IVF clinics.

Important design criteria for the cryogenic system

Phase separator (AKA keepcold, keepfull, cryovent or vapor vent device)

A phase separator is a device that keeps as much liquid nitrogen as possible inside a Vacuum Jacketed (VJ) piping system by relieving the excess gaseous nitrogen. The owner should be mindful of the following factors:

- Although the phase separator provides "liquid nitrogen on tap," it does waste an important amount of gaseous nitrogen out of the piping system.
- In general, phase separators are installed ONLY on VJ piping supplied by a bulk nitrogen system.
- **Owners often complain about the high amount of liquid nitrogen used when the VJ piping is supplied via liquid nitrogen cylinders.** For systems smaller than 100 ft, it is recommended to use smaller diameter inner VJ piping.

Beware of elevators

Carrying liquid nitrogen cylinders or portable liquid nitrogen dewars in elevators is a real safety hazard. Several IVF clinics are located on the upper floors of multi-story buildings.

Some safety recommendations for IVF clinics:

- The safest way to carry these containers on elevators is to have two people; one at the floor level sending the containers, and one at the IVF clinic floor level to receive them.
- No one should be in the elevator while the liquid containers are inside.
- The elevator must not stop to pick up people between the two floors.

What is the problem? Liquid nitrogen cylinders are equipped with low pressure relief valves. The pressure relief valve is releasing nitrogen (an asphyxiant) directly into the air. This creates **oxygen depletion** and poses a risk to anyone inside the elevator.

Keep it short

There are multiple reasons to keep the liquid nitrogen delivery system as short as possible:

- Any type of liquid nitrogen transfer piping, even the Vacuum Jacketed type, will "heat leak." That means the ambient temperature will reach the liquid nitrogen over time. The liquid nitrogen will start to boil off and the pressure relief valve(s) will open.
- Each time liquid nitrogen is used, a certain amount is also used to cool down the pipeline and keep it cold. The amount of liquid nitrogen wasted for that purpose can be kept to a minimum if you keep your piping as short as possible.
- The other benefit of keeping your VJ piping short is the initial investment. The cost of a VJ piping system can range from upwards of $1000+ per linear foot depending upon the size, the length and the complexity of the cryogenic piping.

For VJ piping, the shorter, the better.

About cryogenic freezers

Cryogenic freezers are used for long-term storage whereas portable liquid nitrogen containers should be used to carry semen and eggs from the freezer(s) to the patient(s).

Cryogenic freezers keep liquid nitrogen in their "belly" and replenish the liquid nitrogen level as needed before it runs out. This replenishing process does not have to be done within a pre-determined time frame. **Whether the liquid nitrogen replenishing process is done within 30 minutes or 60 minutes does not matter.**

Controlled-rate freezers

Unlike cryogenic freezers, for controlled-rate freezers, the timing of liquid nitrogen replenishment is very important. Controlled-rate freezers rely on a rapid liquid nitrogen supply. Once the nucleation process is started, the supply of liquid nitrogen must be stable and continuous throughout the entire cycle. **In general, controlled-rate freezers require their own (dedicated) liquid nitrogen supply piping.**

Fully automatic switchover manifolds vs manually operated manifolds

Cryogenic components are expensive. Every new construction project, whether it is an IVF clinic or not, must stay within budget. **There are several questions owners should ask themselves when choosing between a manually operated manifold or a fully automatic switchover manifold:**

a. What is going to happen if the freezers run out of liquid nitrogen?

b. What are the complications if I cannot fill my portable liquid nitrogen dewars if I run out of liquid nitrogen?

c. Is it safe to rely on my supplier to bring emergency liquid nitrogen cylinders?

d. Does my staff have enough time to manage the liquid nitrogen supply?

A manually operated liquid nitrogen manifold puts the burden of making sure the liquid nitrogen supply is adequate for the proper operation of the freezers (if freezers are present) on the personnel. This can be a problem during periods that the freezers will be unattended by personnel, such as long weekends. Fully automatic switchover manifolds are designed to switch from a depleted bank to a full bank without any operator intervention.

Oxygen depletion monitoring

One cubic foot of liquid nitrogen equals 704 cubic feet of gaseous nitrogen. The expansion ratio of liquid to gas is therefore 704:1. Each time a liquid cylinder containing 230 liters enters the IVF clinic, it introduces over 5,000 standard cubic feet of gaseous nitrogen. This gaseous nitrogen will evaporate into the clinic through a pressure relief valve, liquid nitrogen dewars, liquid nitrogen freezers, or controlled-rate freezers. Gaseous nitrogen is not toxic, but displaces oxygen in the air. That's why it is important to have an oxygen depletion monitor properly located in the clinic. Even the best mechanical ventilation system cannot be considered as a safe means to avoid oxygen depletion in any given room in the clinic. **The following tips should be followed while designing for the oxygen depletion monitoring system:**

- **An oxygen depletion monitor shall be installed where the liquid nitrogen source is located** (e.g. manifold room) and another oxygen depletion monitor shall be installed where the cryogenic freezers are located.
- **A warning device** (visual and audible) shall be installed in each room where an oxygen sensor is located (e.g. manifold room and freezer room). Don't forget to install proper **signs** indicating the reason for the alarm.
- The oxygen sensors shall be installed at **eye level.**
- One oxygen monitor covers a **radius of 20 feet.**

Discovery: Contacts

Project name:	Form completed by:	Date:
Project location:	Owner contact name:	Phone number:

Purpose

Discovery is the most important of all phases of an IVF project. This is where we learn the owner's requirements, list of IVF equipment requiring gas or liquid nitrogen, understand why the owner wants what they want, and sometimes more importantly, understand a little of how the owner thinks. It can be the right opportunity to bring new technologies and concepts for the systems to which the owner has had no exposure to.

Gas cylinder supplier

Company name:	Contact name:
E-mail address:	Telephone number:

Liquid nitrogen supplier

Company name:	Contact name:
E-mail address:	Telephone number:

Verifier/Certifier

Company name:	Contact name:
E-mail address:	Telephone number:

Architect firm

Company name:	Contact name:
E-mail address:	Telephone number:

Note : This Discovery Section has been designed for IVF gases and liquid nitrogen. Please use the Discovery Section of the Medical Gas Design Guide by BeaconMedaes for all gases related to patient care.

Discovery: Gas supply for cell culture equipment

Project name:	Form completed by:	Date:
Project location:	Owner contact name:	Phone number:

List of incubators*

Incubator no. or Qty	Make	Model	Size (in cu.ft.)	Carbon dioxide pressure required	Nitrogen pressure required	Gas mixture pressure required

* This table is provided for reference only. IVF clinics own several incubators in various sizes, brands and styles. Knowing how many incubators are using which type of gas will provide you a clue on how big the gas supply equipment will have to be..

List of IVF workstations**

Workstation identification	Make	Model	Size (in cu.ft.)	Carbon dioxide pressure required	Nitrogen pressure required	Gas mixture pressure required

** The number of IVF workstations is relatively limited (anywhere between 2 and 8 depending on the size of the clinic). Make sure to determine which gas will be required at each IVF workstation. It is common to have IVF workstations without any gas supplied to them.

Question	Answer	Why this question?
Do you have a preference between stainless steel and copper to carry the IVF gases from the manifolds to each point of use?		As mentioned in the Important Design Criteria Section on Page 27, stainless steel tubing is recommended as opposed to copper piping.
Do you want to be able to monitor the manifold status and the pipeline pressure remotely?		If the owner already has another IVF clinic, he or she might be surprised by the question as not all existing IVF clinics are equipped with master alarm boxes or area alarm boxes.
Do you want to be able to isolate your piping distribution system by zone?		This is related to whether or not the pipelines will be set as one piping or if zones are required within the IVF clinic.
Who will be responsible for managing your gas supply?		Due to a good working relationship between the gas company and clinic owner, some gas companies will deliver full cylinders and pick up empty cylinders at the clinic site.
Do you have a preference for the pipeline pressure for each IVF gases?		As explained in the Important Design Criteria Section on Page 27, the pipeline pressure should be set at 100 psi. Each point-of-use would be equipped with a pressure reducing regulator to control the pressure individually.

Discovery : cryogenic system

Project name:	Form completed by:	Date:
Project location:	Owner contact name:	Phone number:

List of portable liquid nitrogen open flasks (Dewars)*

Qty	Make	Model	Capacity (in liters)

* This table is provided for reference only. Most clinics own dozens of these portable liquid containers in various sizes and styles. Knowing how many containers are there to be filled will provide you a clue on how big the source of liquid nitrogen will have to be.

List of stationary cryogenic freezers**

Qty	Make	Model	Capacity (in liters)

** Most clinics own only one or two freezers

List of controlled rate freezers***

Qty	Make	Model	Capacity (in liters)

*** Most clinics do not own any controlled-rate freezers. You can expect only one controlled-rate freezer per IVF clinic, if any.

Question	Answer	Why this question?
What is the source of liquid nitrogen?		Very few IVF clinics are large enough to justify a bulk liquid or even a micro-bulk liquid nitrogen storage system. A portable liquid nitrogen cylinder supply system is commonly used by most IVF clinics.
Do you want a filling station for your portable liquid nitrogen dewars?		Some IVF clinics get their pre-filled portable liquid nitrogen dewars through an outside company. Most IVF clinics fill their own portable liquid dewars directly from a liquid cylinder or from liquid nitrogen pipeline.
Do you want to supply your stationary cryogenic freezer via a manual manifold or via an un-interrupted liquid nitrogen source?		Having a piece of equipment that supplies liquid nitrogen on an as-needed basis is the best method to keep semen and eggs continuously frozen. Manual supply systems rely on human monitoring for liquid nitrogen cylinder changeouts.
Do you have a preference for the type of insulated piping carrying the liquid nitrogen (vacuum jacketed or foam insulated)?		This question implies that the liquid nitrogen source will be in a different location than the freezers and dewars. VJ piping requires a significant up-front investment but the payback is less than 3 years compared to foam insulated piping.
Some vacuum jacketed systems come with all items (primarily hoses and valves) insulated under vacuum. Is this what you want?		Many IVF clinics opt for VJ piping but choose non-VJ valves and hoses to minimize the initial capital investment. Although the heat loss is significant, this type of system is better than the foam insulated piping.

List of equipment

Project name:	Form completed by:	Date:
Project location:	Owner contact name:	Phone number:

Gas cylinder discharging equipment

Carbon dioxide manifold	Model number: AFAM1500HB-CGA320-IVF	Quantity
Nitrogen manifold	Model number: AFAM3000B-CGA580-IVF	Quantity
Gas mixture manifold	Model number: AFAM3000B-CGA500-IVF	Quantity

Pipeline accessories

Tie-in kit	Model number: TIK	Quantity (one / manifold)
Zone valve box	Model number: ZVBL	Quantity (one / area)
Hi-low pressure switch assembly	Model number: HLPS	Quantity (one / manifold)

Point-of-use control

Carbon dioxide wall outlet	Model number: WOA-CGA320	Quantity
Carbon dioxide regulator	Model number: MBB-CGA320	Quantity
Nitrogen wall outlet	Model number: WOA-CGA580	Quantity
Nitrogen regulator	Model number: MBB-CGA580	Quantity
Gas mixture wall outlet	Model number: WOA-CGA500	Quantity
Gas mixture regulator	Model number: MBB-CGA500	Quantity

Note : Model numbers for the equipment listed are not complete and are to be used as a reference.

List of equipment

Project name:	Form completed by:	Date:
Project location:	Owner contact name:	Phone number:

Safety and annunciation

Master alarm box	Model number: TOTALALERT INFINITY™	Quantity (one / entire bldg)
Gas monitoring equipment	Model number: FGM	Quantity (one / area)
Audio visual alarm	Model number: SFBH	Quantity (one / area)

Cryogenic piping*

Internal pipe diameter	Diameter:
External jacket diameter	Diameter:
No. of drops	Quantity:
Total length of piping (including drops but excluding hoses and valves)	Quantity:
Vacuum jacketed cryogenic valves	Quantity:
Non-vacuum jacketed cryogenic valves	Quantity:
Vacuum jacketed flexible hose	Quantity:
Non-vacuum jacketed flexible hose	Quantity:
Hose phase separator for dewar filling	Quantity:
Mechanical keep cold	Quantity:

*Please fill out one table per cryogenic system

Note : Model numbers for the equipment listed are not complete and are to be used as a reference.

Engineering specifications

We are confident about the recommendations contained in this guidebook. They are based on years of experience in the field and our equipment have proven over the years their reliability and suitability. Should you require an electronic version of our equipment engineering specifications, you can download them at www.beaconmedaes.com.

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