

Medical Air

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Notes

Notes on Using this Pamphlet:

This pamphlet is presented as a service to producers and users of medical air. We deal here with medical air in its pharmaceutical form Medical Air, USP or Medical Air EuPharm. Our purpose is to discuss the issues surrounding the production in the facility of this pharmaceutical grade gas.

The medical gas pipeline standards referenced herein are primarily the NFPA 99 (US) and the CSA Z7396-1 (Canada). These reference the United States Pharmacopeia (USP) for their purity requirements for medical air. Other standards will be relevant in other locales, as examples the ISO 7396-1 and its many flavours, the AS 2896 (Australia), and the GB 50751 (People's Republic of China). These may reference the European Pharmacopeia (EuPharm) or a national pharmacopeia. The common theme is that all medical gas standards refer to medical air as defined by a pharmacopeia, and therefore all consider it to be a gaseous pharmaceutical. (e.g. Oxygen, Nitrous Oxide, Carbon Dioxide, etc.) Therefore, the standards treat medical air with the same respect.

The user is encouraged to obtain copies of their locally relevant standard or the NFPA 99 or CSA Z7396-1 if they intend to implement such a system in their facility.

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The Companies:

Air Liquide Healthcare is engaged worldwide in the manufacturing and distribution of compendia medical gases. With a dedicated Healthcare World Business Line, we offer patient centric respiratory products and services in over 80 countries, including on-site production of medical air and oxygen at healthcare facilities.

BeaconMedæ's medical air plants serve in the majority of hospitals in the United States, the United Kingdom and many other places worldwide. We are involved in standards development and education for NFPA, ISO, CSA and many other world medical gas standards.

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Comments on this booklet or on any aspect of medical gases are welcome and encouraged. Please send to mark.allen@beaconmedaes.com or paul.edwards@airliquide.com.

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Introduction

In this collaborative paper we examine the medical gas most often taken for granted - medical air.

Because air is compressed in the facility, often by a dusty looking compressor plant down in some rarely visited, dark, uncomfortably hot mechanical room, facilities tend to forget it. But that air is being used to treat patients, to keep them alive - often for extended periods of time. Medical air is most critical to the most vulnerable patients - the heaviest users in many facilities are neonatal, pediatrics and intensive care. Few stop to think that Medical air is the most used pharmaceutical (by volume) in the facility.

Medical air usage rivals and often exceeds the use of oxygen. We take it for granted because we breathe it every minute of every day, but when dispensed from a pipeline in the ICU or the NICU air is an essential partner in virtually every respiratory therapy regime, and there are many life saving therapies which could not be administered without it.

Medical Air USP is identified in the regulations as a drug, just like Oxygen USP or Aspirin USP, or Amoxicillin USP. Yet it's made in the basement under the primary supervision of the facility engineer.

Most facility engineers are astounded to learn that, by volume, they actually are responsible for the number one prescribed gaseous drug in their facility!

What is Medical Air?

So what is medical air? Is it not just regular air delivered at a higher pressure? As engineers, this is how we tend to see it. But when we recognize that by law and by application it is a drug, it makes sense to see it through the eyes of the clinicians. What do they believe is coming from the medical air wall outlet? Why do they use the wall outlet air in preference to room air?

Time and again they use the words "pure" and "medical grade". The expectation is that when medical air is dispensed from the medical air wall outlets, it is "pure" and it is "medical grade". In other words, suited to the use of patients.

We know all "air" is comprised of about 21% oxygen with the balance being largely nitrogen. So what is the difference between room air, industrial or compressed air, breathing air, and medical air? The answer is quality.

With room air and industrial compressed air, you get

what you get (the quality is whatever the intake air contains, plus any contamination that might be added or removed during the compression process). You use it however you wish, but not for breathing. Medical air and breathing air on the other hand are intended specifically for human respiration. They have a minimum quality specification defined in regulations.

In north America, both Health Canada and the US FDA recognize the United States Pharmacopeia (USP) specification for medical air, which defines Medical air as a natural or synthetic mixture of gases consisting largely of nitrogen and oxygen, it contains not less than 19.5 percent and not more than 23.5 percent oxygen by volume, and has:

- no discernible water vapour or oil
- no more than 500 ppm of carbon dioxide
- no more than 10 ppm of carbon monoxide
- no more than 2.5 ppm of nitrogen dioxide
- no more than 2.5 ppm of nitric oxide
- no more than 5 ppm of sulphur dioxide

In most countries medical air is similarly regulated as drug, and therefore has quality requirements defined in the applicable local pharmacopeia.

Throughout this paper, we will refer to Medical Air and Oxygen. When these terms are used, they should be taken to mean Medical Air, USP, and Oxygen, USP - the pharmaceutical versions of these gases.

Why is room air not good enough?

This question takes us back to our discussion with the clinicians, this time to learn what therapies involve Medical Air. Central to this, of course, are patients. Remember, the air you are breathing while reading this paper may be suitable for you, but clinicians cannot (at least should not) assume the same for their patients.



Detail 5.1
A Medical Air Terminal Unit

Historically, the most common use of Medical Air has been aerosol drug therapies. An aerosol treatment involves delivery of a drug, humidification, or both in aerosolised form into the body via the lungs. Since



ADAM.

Detail 5.2

Typical aerosol therapy equipment

clinicians expect piped Medical Air to be of superior quality to room air, medical air has become the standard delivery medium. Aerosol therapies typically consume 4-8 lpm of Medical Air, and last 15-20 minutes. (see Detail 5.2)

Medical Air is also widely used for infant resuscitation. About 10% of newborns have difficulty with their first breath, and clinicians are called to help the babies expand their lungs. The north American protocol for infant resuscitation prescribes the use of Medical Air in preference to Oxygen given the complications associated with pure oxygen and newborn lungs.

Next on the list is high flow therapy. For babies, 1-8 lpm of heated and humidified Medical Air, USP (sometimes referred to as *medical grade vapour*) is delivered via nasal canula to keep the infant's airways open and reduce the baby's work in breathing.



Detail 5.3

Infant High Flow Nasal Therapy

What is Medical Air?

Similar high flow therapies are administered to adults, and require between 10-40 lpm.

Controlling the temperature and breathing environment of both pre-term and full term babies is often critical to the successful treatment for a multitude of conditions. (See Detail 6.1)

In these cases, clinicians employ isolettes, which are commonly supplied with Medical Air, or a mixture of Medical Air and Oxygen.

Flow-rates typically range between 4-8 lpm.



Detail 6.1

A neonate in an isolette

Ventilation of all patient types is yet another common use of Medical Air. In some cases the air is used as a pneumatic drive gas, and in others it is central to the therapy. High frequency oscillating ventilators consume 75-100 lpm of medical air as they deliver respiratory rates up to 4 times normal values (ie > 150 breaths per minute) at very low tidal volumes.



Detail 6.2

Carefusion High Frequency Oscillating Ventilator (HFOV)

And finally, Medical Air is frequently used in lieu of nitrous oxide as an anaesthetic agent carrier gas for

surgeries, especially brain and bowel procedures where the surgeons wish to minimize tissue swelling, a common side effect of nitrous oxide.

General operatory use of Medical Air involves flow-rates between 2-4 lpm, for durations of 45 minutes to many hours.

A technique called *High frequency jet ventilation anaesthesia* is commonly employed for ear, nose, and throat, thoracic, and radiology guided cases. HFJV protocols may consume 75-100 lpm.

As you can easily see, all of these therapies are only possible because Medical Air is readily available, reliable and not one of them would ever be performed if the clinical staff had any reason to assume the air from the medical air outlets was less than “pure” and “Medical grade”

If fact, it is interesting to note that that ventilators and anesthesia machines alike are available with on-board compressors. These models, however, are rarely found where piped Medical Air exists. Why? Because clinicians perceive that wall air is “pure” air and on-board compressor air is simply room air. It is seen as a possible source of airborne infection.

As facility engineers we know where the Medical Air plant can be found. But the clinical staff usually does not. The majority of clinicians believe it comes from commercially produced cylinders, like Oxygen or Nitrous Oxide, because they see these cylinders every day. For small users, like a clinic, this may actually be the case. A well designed and maintained manifold to control and deliver Medical Air from high pressure cylinders makes perfect sense when usage is small.

We try to following the rule of thumb that tells us to fit headers with enough cylinders to last a week or more, but as usage rises, the acreage required and the management headache for the cylinders, the reserve cylinders and the empties starts to get impossible.

Replacing empty cylinders is a dirty, labor intensive, hands-on job, so long before the space requirements get unmanageable, the agony of constantly switching cylinders has made Medical Air via manifold very unpopular.

So, for most facilities, demand renders high pressure cylinders impractical, both to buy and to manage. Pure gases, such as Oxygen, Nitrous Oxide, and nitrogen can be readily scaled (i.e. high pressure cylinders yield to portable bulk cylinders which again may yield to stationary bulk tanks as the demand

gets larger). Mixed gases such as Medical Air are not so easily scaled. So in most healthcare facilities, the Medical Air dispensed from wall outlets can only be manufactured on-site.

Medical Air is produced in one of two ways. (and this is true whether it's done at the hospital or done at the gas company to fill those cylinders)

- 1) Air is compressed using a compressor system which draws outdoor air as their raw material (known in the pharmaceutical business as the “active pharmaceutical ingredient (API)”); or
- 2) Oxygen, USP and Nitrogen, NF are the “API” and are blended in proportions containing not less than 19.5% and no more than 23.5% Oxygen. This is “synthetic air”.



Detail 7
A Complete Medical Air Plant

Although they are encountered in Europe, Brazil and Japan for example, the use of proportioning systems to create synthetic air on site at a healthcare facility is quite rare. The quality of synthetic air is brilliant, but the cost per liter is painful. As a simple matter of economics, synthetic air is impractical anywhere that the regulatory environment does not absolutely mandate that extreme purity.

As a result, compressor plants are the standard method for onsite production everywhere.

Commercial versus on-site Medical Air.

What is the difference between commercially produced Medical Air and the product made on-site at hospitals? Other than pressure, it's all about quality

control and the legal environment wrapped around it. In order to have Health Canada or FDA blessing to release the product to market, commercial producers of Medical Air must comprehensively test each batch against the USP specification, and release only those batches that conform. They must record the result and be able to trace where every liter of gas from the batch was sent. If there ever is a question, they have full traceability of the drug they have made. FDA in the US and Health Canada monitor these manufacturing plants closely, ensuring they are following “Good Manufacturing Practice” (GMP) when these drugs are made and distributed.

When the drug is made in the basement of the hospital, in theory your facility has become a drug manufacturer and could be expected to follow the same guidelines and undergo the same inspections. However, as long as you make the drug only for use in your facility, and don't package or sell it to others, neither of these regulatory agencies has elected to require this of you.

On-site Regulations

That is not to say there are no rules at all. First and foremost, it is common rule that all drugs dispensed within a hospital must be listed within the hospital's formulary. Medical Air is no exception. In north America, hospital formularies should always include all the gaseous drugs, Medical Air, USP included, if they intend to perform any respiratory therapies using it.

The listing in the formulary is a legal obligation of the pharmacist, and both allows and requires a product meeting the formulary specification to be dispensed.

The underlying assumption of the regulators is that you will follow the appropriate NFPA and CSA standards. These are the primary guides that provide for a minimum of quality control. The quality assurance requirements in these standards are limited – selection of intake location to ensure best available outdoor air, oil free or oilless compressors, continuous monitoring of Carbon Monoxide and dew point, and periodic checking (generally an annual test) of the other parameters of the USP.

On Site Considerations

There are many, many other considerations in maintaining air quality from an onsite production facility. The selection of compressor technologies, the operating modes, the choice of filters, etc. etc. all have an influence on the ultimate quality of the

Medical Air Quality

product drug, and the manufacturer – the facility engineer – needs to be aware of all of them and how they interrelate.

Let's return to the intake as an example. If you take an air system fully compliant with CSA or NFPA standards, and you hook the exhaust from a diesel truck to the intake, what will happen?

Leaving off the sugar coating, the simple reality is that patients will be breathing diesel exhaust in a matter of minutes. The only notification you will receive will be the Carbon Monoxide alarm.

What is drawn in the intake is what will go to the patient.

Now, our example is extreme, admittedly. But it is not as ridiculous as one might think. It has occurred that the intake is located too near the loading dock, and the pollutant levels rise every time the dock is occupied (this finding was one of the original motivations for adding the CO monitor to the standards). It has also been the case that the intake air quality was compromised by the local environment (e.g. local air pollution, a forest fire or even a fire in the building itself).

Intake location is (after selection of the compressor itself) the most important element in assuring air quality. To borrow Lincoln's famous aphorism: clean air is available to some of the world, all of the time, and clean air is available to all of the world, some of the time, but clean air is not available to all of the world, all of the time. Locating the intake is all about making sure we have the very best chance at "all of the time" for our facility.

This brings us back to the topic of Good Manufacturing Practices, or GMP, at the heart of which lie three basic tenets:

Quality assurance (Q.A.), the maintenance of a desired level of quality in a service or product, especially by means of attention to every stage of the process of delivery or production. and

Quality control (Q.C.); a system for verifying and maintaining a desired level of quality

The NFPA and CSA medical gas piping standards address both of these, with fine prescriptive language to satisfy the quality assurance element, and objective, (a.k.a. performance) instructions for quality.

The third basic tenet of GMP is Validation. This is

where we double check and document our Q.A. and Q.C. to substantiate we built the system we intended and it produces the quality of product we set out to make. Q.A. validation of medical air systems in North America is well established, involving third party inspection and verification of system design, installation, and operation.

Validation of quality control has room for improvement. Before first use, the same inspection bodies doing the Q.A. verification take a gas sample from the main feed line and have it tested. The result is normally a passing grade, which tells the facility engineer at the time of startup, all was good. This test might be repeated on some calendar basis (every 6 months or 12 months are typical timeframes). We therefore know for that moment in time what the medical air quality was. However, the the design standards may ensure our odds are the best they can be, but we cannot control the quality of the outdoor air at the intake, which is the air compressor system's "raw material (API)" in pharma terms. Perhaps for the sake of patients being treated with medical air a more robust QC program should be considered.



Detail 6.2

Typical CSA Medical Air System complete with Air Liquide Healthcare's aerALin™ Quality Control Module

Quality in, quality out?

So with a proper respect for Medical Air, would we be remiss in assuming the quality of air coming from the wall outlets matches what enters the pipeline? Indeed, assumption is nearly always a culprit in poor quality.

Medical Air pipelines are part of the physical fabric of the building. The compressors, dryers, filters etc, may,

and normally do, change throughout the hospital's lifetime. The pipeline by and large ages with the building. We could compare it to a human heart, lungs, and vascular system. We sometimes replace the pump and filter, but swapping arteries and veins is simply unrealistic.

So it is vitally important to give your pipeline a regular check-up. Sampling from random outlets may reveal sections with accumulated moisture or gas cross contamination caused by malfunctioning blenders.

The final piece: What's your plan?

As a facility engineer you are charged with producing a therapeutic product for which patient care is highly dependent. Do you have a plan encompassing all elements of your responsibility?

Here are some questions to consider in developing your overall medical air production plan:

1. What is the demand for Medical Air in your facility? Which departments use it, for what therapies, and with which medical devices?
2. What level of purity is required (ie what is listed in your formulary)? For example, is the NICU ok with 500ppm of CO₂, or would they prefer less than 50 ppm?
3. Is your Medical Air system designed in a way that allows it to continue meeting peak demand whilst one pump is removed for service? How about two pumps removed for service?
4. Does your purification system result in the quality required by your clients?
5. Does your quality control system meet hospital standards?
6. Does your quality control records retention meets hospital standards?
7. What is your plan should normal power be interrupted?
8. What is your plan should emergency generators not start, or cease to operate?
9. Do you have reserve bank of high pressure cylinders labelled as containing Medical Air, USP?
10. Given normal demand, how long will your reserve cylinders last?
11. Do you maintain extra stock high pressure cylinders for your reserve manifold, and are you in sync with your gas supplier's ability to replenish this stock?
12. Do you maintain stock of portable high pressure cylinders, labelled as containing Medical Air, USP, together with regulators, carts, and wrenches?

References

- CSA Z7396-1 2012 Medical Gas Pipeline Systems
Canadian Standards Association, 178 Rexdale Blv'd,
Toronto, ON Canada M9W 1R3
- NFPA 99 2015 Healthcare Facilities Code
National Fire Protection Association
1 Batterymarch Park
Quincy, MA USA 02169
- USP29 – NF24
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