Why Laboratories are Choosing Gas Generators Over Gas Cylinders

Pharmaceutical laboratories use a variety of analytical techniques as part of research and development and quality control of products. Many of these processes require high-purity gases, many of which can be produced by gas generators. For a number of reasons, including safety, cost and convenience, more and more laboratories are abandoning gas cylinders in favour of gas generators to supply the gases they require for their analyses.

Two gases which are often supplied via gas generator are hydrogen and nitrogen. Hydrogen gas is typically used for applications such as GC (gas chromatography) and ICP-MS (inductively coupled plasma mass spectrometry) while nitrogen can be used for a variety of applications including LC-MS (liquid chromatography mass spectrometry), sample evaporation, NMR (nuclear magnetic resonance) and ELSD (evaporative light scattering detectors).

About Hydrogen

Hydrogen was discovered by Henry Cavendish in 1766 and it is the most abundant element in the universe, essential to all life as we know it. On earth, it is the third most available element, although in its gaseous state it does not naturally occur, and must be manufactured. It is combined with oxygen to create water (or H_2O), a necessity of all life on this planet. Hydrogen gas has been used for numerous applications in industrial manufacturing and processing, most famously in the Haber-Bosch process for ammonia production, but also as shielding gas in arc welding as well as numerous laboratory applications, such as its use for detector and carrier gas in gas chromatography.

How Hydrogen Gas Generators Work

Hydrogen gas generators electrolyse deionised water to its constitutive elements, oxygen and hydrogen, via a proton exchange membrane (PEM). Hydrogen ions diffuse through the PEM membrane, before combining to form hydrogen molecules, whereas oxygen is retained and then vented to atmosphere. The hydrogen molecules which form, drag some moisture through the PEM cell and require further purification via a desiccant drier or pressure swing adsorption (PSA) drier before being supplied to the application.

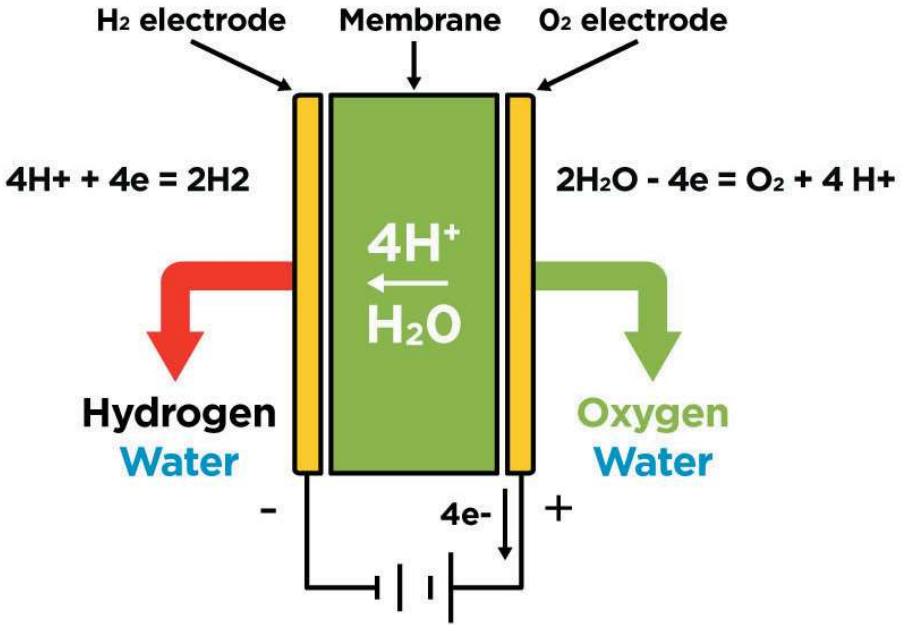


Illustration of electrolysis in a PEM cell

Why Laboratories Use Hydrogen Gas Generators: Cylinders vs Generators

Many laboratories are now prohibited from placing hydrogen cylinders on their premises owing to health and safety restrictions. Hydrogen cylinders can contain up to 9000 litres of gas, more than enough to cause a significant explosion or fire. Hydrogen generators, which produce hydrogen on demand and therefore contain only a minimal amount of gas, are much safer than cylinders and have increasingly become the alternative of choice for many.

Hydrogen generators eliminate the need for:

- **Cylinder changes** – gas cylinders require frequent replacement and this can interrupt analyses, while also increasing the risk of contamination through ambient air entering the system. Cylinder changes also require laboratory staff to manually handle and move the cylinders, which comes with an inherent risk of accident or injury.
- **Cylinder storage** – when using gas cylinders, a laboratory needs to ensure that its supply provides enough gas for their analyses. Not only is this a space issue, it is a potential safety issue since storing large quantities of an explosive gas can be extremely dangerous.
- **Cylinder monitoring** – gas cylinders need to be continually monitored to avoid the gas supply running out mid-analysis.

When compared to the costs of gas cylinders, which include the cost of gas, delivery charges, cylinder rental charge, staff downtime, administration, occupational health and safety measures and training, a hydrogen generator can typically pay for itself within nine to 15 months.

Why Laboratories Use Hydrogen Gas Generators: Helium vs Hydrogen

For GC users, where helium has traditionally been the carrier gas of choice, hydrogen can provide a more economical, safer and in many instances faster carrier gas. Helium is a finite resource and must be extracted from earth using large-scale industrial processing facilities, dispensed into cylinders and shipped to a laboratory. As a commodity, helium cost is subject to supply and demand fluctuations and, whilst global supply is dwindling, demand remains strong, meaning laboratory users of helium have had to endure ever-increasing prices to supply their labs.

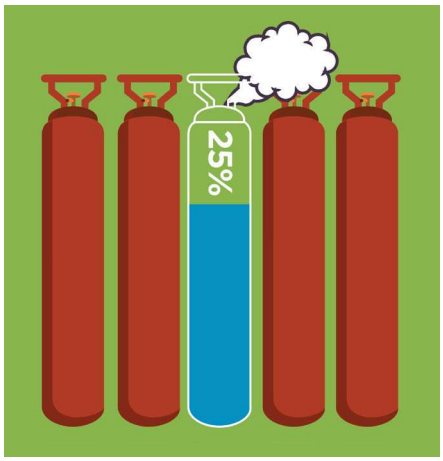
Supply issues have also been a major concern for laboratories and other helium-reliant applications (such as hospitals with MRI scanners). Qatar, the world's second-largest source of helium supply, recently had its land trade routes blocked as part of a dispute with Saudi Arabia. It took over two months for supply to re-enter the market through a new, longer and more expensive route over sea. This caused disruption to the supply chain and increased overhead costs for suppliers, which trickled down to the end users; laboratories and hospitals.

Producing high-purity hydrogen using only deionised water, a hydrogen generator removes the uncertainty of fluctuating helium costs and unreliable supply.

Hydrogen Safety

The most significant risk with hydrogen use is a leak into the laboratory environment raising the hydrogen content to an explosive level. The safety benefit of a generator can be seen by looking at a theoretical example. The lower explosive limit (LEL) for hydrogen is 4.1% in air. Therefore, the LEL of a hermetically-sealed laboratory of dimensions 5m x 4m x 2.5m with a volume of 50m^3 can be reached by emptying 25% of a 50L cylinder of hydrogen. With a large enough leak this can be achieved in minutes.

High-pressure hydrogen can also undergo auto-ignition when released rapidly from a cylinder. Hydrogen generators are generally designed to contain a minimal amount of hydrogen. For example, with a hydrogen generator which contains <400cc of hydrogen, it would take nearly 12 days to reach the LEL in the same lab, and would require the entire volume of the highly diffused gas produced to remain within the room.



Just 25% of a 50L hydrogen cylinder could be enough to cause an explosion

About Nitrogen

Nitrogen was discovered in 1772 by Daniel Rutherford. As an inert gas, it does not react readily with other elements and chemicals. It is highly abundant, accounting for around 78% of the earth's atmosphere, meaning we breathe in more nitrogen than any other element. Since its discovery, nitrogen gas has been used for a variety of important functions. Its inertness enables it to provide important protection for industries where oxidation is undesirable, such as food packaging, reducing fire hazards, manufacturing of stainless steel, wine bottling, chemical analysis and, in particular, for LC-MS and GC.

How Nitrogen Gas Generators Work

Nitrogen generators use a supply of dry, oil-free air to purify nitrogen via a selectively permeable membrane or carbon molecular sieve material which removes oxygen, carbon monoxide and carbon dioxide. Purified nitrogen is then stored in a buffer tank to ensure constant flow and pressure of nitrogen is supplied to the application.

Why Laboratories Use Nitrogen Gas Generators

For many laboratories it is simply more cost-effective to use a nitrogen gas generator rather than nitrogen gas cylinders. A 2010 study by the European Industrial Gases Association estimated that gas supplied from a nitrogen generator used 30% less electricity per volume at 99.9% purity than a nitrogen production plant. For analysts using 98% pure nitrogen, the costs of production from a generator are up to 70% lower, creating significant savings on energy costs, and helping the environment. An LC-MS using 32 litres per minute (1.13 CFM) of nitrogen for eight hours per day will consume around 5.5 million litres (194,230 ft3) of nitrogen in one year of operation. This is equivalent to 620 cylinders. The cost of satisfying such a need for

When air enters a selectively permeable membrane, oxygen particles escape while nitrogen particles remain.

gas cylinders includes the time taken for ordering, cylinder installation, processing of paperwork on top of the cost of the gas itself and the rental of the gas cylinders.

Comparing the example above with the costs associated with the purchase, installation and running costs of a gas generator producing 32 litres per minute (1.13 CFM) of nitrogen to supply the LC-MS, the generator would typically have paid for itself within one year, making it a cost-effective alternative for laboratories using gas cylinders. Nitrogen generators also remove the risk of sample contamination, which is present when using gas cylinders because of their diminishing purity as they empty or the occasional bad-quality cylinder. Generators, through providing a consistent, convenient, and more energy-efficient nitrogen gas supply, can be a great benefit for laboratories.

Nitrogen Safety

Changing over nitrogen cylinders poses a significant safety risk which labs can avoid by using gas generators to supply their instruments instead. For lab managers this is a growing concern, as lab workers carrying awkward and heavy cylinders around a lab are, quite frankly, an accident waiting to happen. Cylinder handling, as previously mentioned with helium and hydrogen cylinders, requires occupational health and safety training for lab workers in order for handling to take place. Even with training, cylinders still pose a significant health risk in the laboratory or any workplace where they are used.

Should a cylinder be damaged or leak and quickly release a large amount of nitrogen into the laboratory, there is a risk of asphyxiation. This risk isn't present with nitrogen gas generators, which only store a minimal amount of nitrogen, insufficient to present a risk of asphyxiation. Furthermore, a generator will not contain gas at the same high pressure as it would be contained within a cylinder.

Gas Generator Safety Technology

Hydrogen and nitrogen generators on the market today contain a wide range of technologies to ensure user safety. Technologies such as forced air ventilation, internal leak checks, automatic shutdown and pressure sensors are all designed with safety in mind – their main priority being to prevent a dangerous amount of hydrogen or nitrogen from building up within, or being released by, the generator.

GC Applications in Pharma where Nitrogen or Hydrogen can be Used

A large number of gas chromatography (GC) methods use nitrogen carrier gas and flame ionisation detection (FID) for analysis of both active ingredients, such as alpha tocopherol (Vitamin E) and atropine, and for determination of safe levels of formulants or chemicals used in the process of drug formulation, such as stearic acid and solvents. Nitrogen or helium are preferred for use as carrier gas in pharmaceutical analysis because of their inertness, which means that they will rarely interact with active ingredients.

The United States Pharmacopeia (USP) chapter 467 details the analysis of residual solvents in pharmaceutical products and is used to determine the presence of solvents even without prior knowledge of their use in the manufacturing process, since the manufacturing processes of different companies may use different solvents. Residual solvents are defined as organic volatile chemicals that are used or produced in the manufacture of drug substances, or in the preparation of drug substances.

Residual solvent analysis (RSA) uses static headspace extraction GC-FID for separation and detection of solvents. The method for RSA, in accordance with the USP, requires the use of either nitrogen or helium as carrier gas and the FID will require hydrogen flame gas along with air or zero air flame support gas.

The ASTM method, F 1884-04, for residual solvent analysis in pharmaceutical packaging material, does not define a carrier gas. This means that labs can choose the most optimum and efficient gas for their analysis. There are clear advantages to be found from opting for hydrogen carrier gas for GC in this circumstance, with faster run times allowing higher sample throughput as well as the aforementioned benefits of replacing increasingly expensive helium cylinders with a hydrogen generator.

With the safety, cost and workflow benefits a gas generator can supply to laboratories when compared with gas cylinders presented, it is easy to see why many laboratories are choosing to replace their laboratory gas cylinder supply with a gas generator. The pharmaceutical industry, particularly those working with packaging materials, have a decision to make: continue with the hassle of gas cylinders, or improve workflow and safety in the lab with a gas generator.

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