Specialty Gases

Added value in pharmaceuticals

By Stephen B. Harrison

What makes a specialty gas special? In some cases, it is a high purity, premium grade of a regular product such as nitrogen. It can also be due to its application in the laboratory and R&D applications, where specialty gases are often used. Or, it might be an exotic chemical gas beyond the regular scope of industrial and medical gases.

In the pharmaceutical sector we can explore examples of all three of these cases to understand how specialty gases are adding value – both to end-users and our industry.

Premium quality adds value

A challenge that many industrial gases business leaders face is how to add value and maintain the price point for common gases, in the face of increasing competition and commoditisation.

A direction that is possible in the pharmaceutical industry is to put more value into the product and thereby exchange more value with the customer. Specifically, this is possible by offering premium certification levels on bulk liquid gases to guarantee that the product batch is suitable for pharmaceutical applications.

The most common gas used in the pharmaceutical sector as a processing aid is nitrogen. Nitrogen is used as a blanketing gas, purging gas and also as a gas to move the product. To ensure that the nitrogen will be of a suitable quality – equivalent to an API – the US, European and Japanese pharmacopeia have established precise criteria that the nitrogen must meet. Additionally, the European Pharmacopeia has a grade referred to as 'Nitrogen, Low Oxygen' that is aligned to 'inerting finished medicinal products' – or pharmaceuticals packaging. These grades should not be confused with the specifications for medical oxygen or medical nitrous oxide, which are relevant for gases which are breathed by patients in hospitals or home healthcare applications.

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Mark Asciak, Commercial Manager at Multigas Industrial & Medical Gases in Malta, explains how his team work with pharmaceutical grade nitrogen. "The pharmaceutical industry in Malta has grown due to the country's geographical location, qualified workforce and well-established Medicines Authority. Multigas has supported the development of the pharmaceutical sector with the supply of GMP (Good Manufacturing Practice) specification nitrogen."

"This goes beyond paperwork, we have implemented robust operational practices to ensure the required quality is achieved and maintained."

Starting from the air separation unit (ASU) at Multigas, the production process is designed to meet GMP requirements and is monitored to ensure that the product is within the European Pharmacopeia monograph. Safeguards are also built into the downstream process and tank farm to ensure product integrity is preserved through the value chain. Furthermore, all employees and subcontractors handling the pharmaceutical grade gases undergo regular GMP training to understand the relevant procedures and to be aware of the importance that these products have in customer processes.

Asciak continues, "The value-add of the premium pharmaceutical grade nitrogen is embodied in the Certificate of Analysis that is issued upon lab analysis of each full tanker prior to delivery. Rather than purging road tankers between industrial and pharmaceutical nitrogen deliveries, the whole tanker fleet is continually maintained at the pharmaceutical level of integrity to ensure consistency."

The Multigas operating philosophy combines local presence with global support. Asciak explains how they have been able to integrate specialty gases into their offer, "Although the Maltese market is limited in terms of scale, over the years we have provided our customers with a robust and reliable supply of gases. We have continually invested in local production of the essential gases and distribution assets to have control over the supply chain."

Clinical sterilisation chamber

Pharmaceutical packaging

"Furthermore, we have also nurtured strong relationships with international gas companies with whom we have arrangements to back-up our gases supply while our plant is undergoing maintenance. They also supply us with exotic specialty gases which enable us to support other pharmaceutical processes such as lab analysis."

All in all, it adds up to a stronger business model for Multigas. "Through our touch points in commercial, logistical, technical and quality areas, we can understand how our gases fit into customer processes and support them with the appropriate products and services. With the pharmaceutical grade gases, the additional complexity and effort that we put in is rewarded by the way we can differentiate our products and the long-term relationships that we can develop with our pharmaceutical customers."

Specialty gases in the lab – make or buy decisions

In pharmaceutical laboratories, it is increasingly common to use laboratory gas generators to make hydrogen, high purity air and nitrogen in-situ.

This either substitutes or compliments the purchase of industrial gases from cylinder or bulk supply modes. Hydrogen is commonly used as an FID fuel gas or GC carrier gas, especially in environmental or hydrocarbon processing applications. Nitrogen is used to support high performance liquid chromatography (HPLC), which is one of the most common separation techniques used in pharmaceutical laboratories.

When HPLC is connected to a mass →

spectrometer to create a LC/MS there is a requirement for high purity nitrogen to act as a nebulising gas. This is also sometimes referred to as drying gas, sheath gas or curtain gas. LC/MS and related variants, such as LC/MS/MS, TOF and ion trap, are the main applications for nitrogen generators in pharmaceutical laboratories. Beyond HPLC, nitrogen can also be used for Evaporative Light Scattering Detectors (ELSD), sample preparation and solvent evaporation.

For the LC/MS instrumentation configuration, typical nitrogen flow rates are 30 litres per minute (lpm) at a pressure of 6-7 bar. The gas must be dry and free of hydrocarbons and particulates. An oxygen concentration between 1% and 3% is acceptable because the MS detector is not sensitive to oxygen. For these reasons, the use of a membrane nitrogen generator is a highly cost-effective gas supply option.

Gerard Catchpole, European Sales Manager – Gas Division at VICI AG International, commented that "at VICI DBS we manufacture a range of nitrogen generators that exceed the requirements of all the major LC/MS manufacturers: leading scientific instrumentation companies such as Sciex, Agilent, Waters, Thermo, Shimadzu and Bruker."

He went on to explain that, "there are two main laboratory nitrogen generator groups. Firstly, nitrogen generators that are fed from a separate supply of high purity compressed air. These generators use membrane technology to convert the compressed air into LC/MS grade nitrogen. There are no moving parts, no noise and no electrical requirements, which makes the generators ideal to be installed directly next to the LC/MS. Flow rates are up to 120 lpm so, up to four LC/MS instruments can be supplied from one generator."

"The second category are complete 'plug and play' nitrogen generators which are required in laboratories where there is no 'on-tap' supply of compressed air available. These fully integrated systems use low noise, oil free compressors to supply air to the nitrogen purification membrane."

Pharmaceutical biotechnology

Achieving diversity

Including a range of refrigerant or chemical gases in the market offer has been an established strategy of several industrial gases suppliers in recent decades. The product mix diversification can support growth and maximise convenience for customers.

On the other hand, chemical gases are often flammable, corrosive or toxic and require sophisticated operations and a robust product stewardship programme. When considering the combined cost, risk and reward, the chemical gases product group may represent an attractive portfolio diversification opportunity for advanced industrial and specialty gases businesses.

In the pharmaceutical sector, some chemical gases are essential building blocks for active ingredients in medications, others are used as processing agents. Ethylene oxide plays a vital role in the sterilisation of pharmaceutical products and medical devices. As an alternative to the use of high temperature/high pressure steam in an autoclave at temperatures up to 130°C, ethylene oxide can be used for low temperature sterilisation at temperatures of 25-60°C. This enables plastics, rubber, resins and other temperature-sensitive materials to be treated without physical deformation.

Alan Watkins, Executive General Manager at Coregas, picked up the thread. "The pharmaceutical sector and hospitals require a range of medical, industrial and specialty gases. To provide an integrated service to the healthcare sector in Australia, we offer essential pharmaceutical and clinical specialty gases, such as ethylene oxide, in our product mix," he said.

"At Coregas we refer to ethylene oxide for sterilisation as 'Biosterile 9' because it is a 9% mixture of the active ingredient in a carbon dioxide carrier. We supply it in this diluted form so that the mixture can be categorised as a non-flammable product which makes storage and usage safer. This blending activity ultimately adds value because it simplifies the supply chain and reduces the costs for all parties involved in the handling and application of this gas."

About the author

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