The new Oxygen 98 monograph and beyond

Electrolysers, two-stage PSA and NASA's Medical Ceramic Oxygen Generator

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Medical oxygen concentrators produce gas in-situ. The concentrator is a certified medical device, and the oxygen purity is continuously measured. Medical oxygen generated by a hospital in this way for its own use requires no marketing authorisation.

For context, cryogenic air separation units (ASUs) produce oxygen which can be allocated to medical applications. In this case, the oxygen requires a marketing authorisation because the medical oxygen gas, not the oxygen generation equipment, is the subject of control.

These details, terminology and many more technical points related to production and quality control are covered in medical oxygen monographs. These documents form part of the US, European and Japanese Pharmacopeia and are akin to specifications or standards to produce medicinal gases.

Mind the gap

O93, the EU Oxygen 93 Monograph (2455), refers to oxygen produced on a molecular sieve pressure swing adsorption unit (PSA) with a target oxygen purity of 93%. It has a tolerance of plus or minus 3%, limiting the upper purity at 96%.

O99.5, the EU Oxygen 99.5 Monograph (0417), stipulates that the minimum purity of medical oxygen produced on industrial cryogenic air separation units must be 99.5%. The US pharmacopeia is similar in many respects, except the minimum oxygen purity for air separation is slightly lower at 99%. Clearly, there is a 'gap' between 96% and 99%, or 96% and 99.5%.

During the Covid pandemic, every effort has been made to boost the availability of oxygen to patients. Modern PSA equipment is capable of producing oxygen at 98% purity, or O98, through a two-stage process. In comparison to 093, O98 is not a medicinal benefit, because in both cases the oxygen is significantly diluted to around 35% during breathing by the patient. But it was proposed that expansion of the permissible oxygen range would allow additional equipment to be used in hospitals, relieving the strain on oxygen supply chains, and enabling more Covid patients to receive therapeutic medical oxygen supplies.

Considering the situation and with a desire to 'close the gap', the European Directorate for the Quality of Medicines (EDQM) felt that the introduction of a new medical oxygen monograph, O98 or Oxygen 98, would be beneficial.

The consultation process with industry experts to receive feedback on the first draft began in April 2020 and by October 2021, the proposed draft monograph was published in the Pharmaeuropa for wider review within the medical community.

Technologies for tomorrow: beyond the Oxygen 98 monograph

The draft Oxygen 98 monograph refers to oxygen produced on 'double-stage concentrators by two successive modules of adsorption purification of ambient air using zeolites'. With such a narrow definition of the production technology, the scope of the O98 monograph to increase the available oxygen supply will be limited.

NASA's Medical Ceramic Oxygen Generator, or M-COG, is also lined up to save lives. John C. Graf, an Engineer at NASA's Johnson Space Centre in Houston, has been leading its development and confirms that "we have developed this technology to the point that NASA is seeking collaboration partners. Partners are essential to scale and commercialise the technology, making it a viable product for use in hospitals."

The M-COG uses a ceramic ion transport membrane, which allows oxygen ions to migrate from process air, across the solid ceramic, into an oxygen storage tank. Pressurised oxygen is generated electrochemically. Oxygen purity is greater than 99.9%, with only an oxygen ion able to pass through the ceramic membrane. NASA is prototyping an M-COG with a delivery pressure of five bar and conducting research on a new type of ceramic oxygen generator capable of delivering oxygen at 150 bar without the use of mechanical compressors.

"The M-COG has only one moving part – the process air fan", says Graf. Unlike the PSA generator there are no changeover valves, so maintenance is simplified. The M-COG does not rely on molecular sieves for adsorption and gas separation, so it is not impacted by altitude nor high humidity in the air.

Graf adds, "A doctor who treats children at a clinic in Papua New Guinea contacted me to put his name at the top of the waiting list for a commercial version of our unit. He believes that the M-COG will solve the problems he has experienced with other onsite oxygen generators. And, where he is located, liquid oxygen or cylinder deliveries would be impossible."

Tapping into NASA's expertise with electrolysis

M-COG is not the only technology that can support the growing demand for medical oxygen. Thousands of tonnes per year of oxygen will be produced by hydrogen electrolysers as a 'free' by-product in the future as green hydrogen plays a leading role in the energy transition.

On the International Space Station (ISS), water is split by electrolysis to generate oxygen for the astronauts to breathe. When large quantities of oxygen are required in outer space for long duration missions, NASA has established that transporting water for electrolysis is more efficient than launching compressed oxygen or liquid oxygen tanks into space.

Through his work at NASA, Graf has decades of experience with electrolysis, and he adds that, "deep space is not the only place where people rely on electrolyser oxygen to breathe. Submarines in the deep sea also use them."

Graf's work at NASA has also involved providing technical support to PEM electrolyser stacks used on nuclear submarines to enable them to

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operate with extended dive periods. "As with the ISS and its large solar panels, on nuclear submarines, electricity is abundant, but oxygen becomes depleted. So, despite its high electrical power consumption, an electrolyser can be a good technology to top up the oxygen levels and ensure the team on board stays safe."

If electrolyser oxygen is good enough for submariners and astronauts, there is hope that it will be suitable for medical purposes also. Using an electrolyser primarily for oxygen generation is more power intensive than the M-COG method, pressure swing adsorption and cryogenic techniques. However, if the oxygen is recovered as a by-product of hydrogen generation on the electrolyser, it can be regarded as a very low-cost and efficient oxygen generation mode.

Electrolyser technology for today and tomorrow

Conventional electrolysers that are built for low-cost hydrogen production generally produce hydrogen at 99.999% or 5.0 grade purity from the electrolyser, followed by a de-oxo unit and dryer. Oxygen, in contrast, is generally produced at only 98% purity, with hydrogen being the main impurity.

Industrial oxygen from ASUs is generally produced at around 99.6% purity. Ultra-high purity oxygen for specialty gases or electronics applications requires 5.0 grade pure oxygen. Some companies, such as Teledyne Energy Systems, offer an oxygen purification module that can be used after their electrolyser to ensure that the oxygen can be produced at these commercial purities.

At 99.999%, the purity of oxygen flowing from the Teledyne unit far exceeds the O99.5 monograph for oxygen produced on a cryogenic ASU. However, as with all purity specifications, the nature of the impurities is what often matters the most. The medical community would naturally wish to undertake clinical trials to demonstrate that the tiny residual amount of hydrogen is not harmful to human health.

Electrolyser technology is innovating rapidly. One of the companies at the vanguard is CPH_2 in Ireland. Its Membrane-Free Electrolyser™ produces a gas mixture of hydrogen and oxygen known as HHO. This is a characteristic of electrolysers that have no membrane to separate the oxygen and hydrogen within the electrolyser stack.

To separate the oxygen from the hydrogen, CPH_2 has implemented a cryogenic process. Like cryogenic air separation where nitrogen and oxygen are purified by distillation, the difference in the boiling points between hydrogen and oxygen also allows for 5.0 grade purities of each gas to be produced. Whether or not this method will be regarded as compliant with the EU O99.5 or US O99 monographs today, will be interesting to consider.

Advances in technology are creating the potential to generate additional low-cost oxygen molecules that could benefit millions of people. Regulations must continuously evolve to enable the use of appropriate innovations and it will be advisable to start work on the next round of Pharmacopoeia regulatory developments now to ensure that high quality medical oxygen from a range of sources is soon available and affordable all around the world. gw