Gas and technology solutions for the biopharmaceutical industry.

Partner of choice.
### Long-standing partner to the pharmaceutical industry

Delivering innovations tailored to evolving market needs.

We have been supporting the pharmaceutical industry with pharmaceutical-grade gases, specialty gases and industrial gases for many decades. Building on our long-standing relationships, we have gained an in-depth understanding of the pressures facing biopharmaceutical companies in such a strict regulatory and competitive environment. As a result, we have developed a number of gas-enabled innovations that help our customers meet increasingly stringent environmental legislation, improve process quality and increase cost-effectiveness.

**Our experts can help you with all your gas supply and management needs across the full biopharmaceutical process spectrum:**

- Improving freeze drying of valuable biologicals
- Processing innovations for ozonolysis, inerting, purging, charging and mixing
- Cooling and freezing for reactors, samples and valuable products
- Tailor-made, tested and traceable gases and supply concepts
- Gas distribution systems to fit purity and performance needs
- Sustainable solutions for emissions and wastewater management
- End-to-end service portfolio covering safety, training, analysis and gas management

### Evolving market

The pharmaceutical industry is evolving beyond traditional pharmaceuticals towards the full integration of biological drug production. It is expected that, within the next decade, more than half of all manufactured drugs will be processed through a freeze dryer. Technology solutions to meet these needs and competitive pressures. Many processes in the manufacture of active pharmaceutical ingredients (APIs) and pharmaceuticals – including R&D, production and quality control – rely on gases (whether pharmaceutical-grade, specialty or industrial). With our expertise, specialised technologies and full range of gases, we can help improve the safety, quality and efficiency of your biopharmaceutical processes.

**Preferred partner for gas solutions**

Gases are employed in various biopharmaceutical steps to meet these needs and competitive pressures. Many processes in the manufacture of active pharmaceutical ingredients (APIs) and pharmaceuticals – including R&D, production and quality control – rely on gases (whether pharmaceutical-grade, specialty or industrial). With our expertise, specialised technologies and full range of gases, we can help improve the safety, quality and efficiency of your biopharmaceutical processes.

A broad portfolio of innovative gas technologies and cryogenic solutions makes us the gas solutions provider of choice for the biopharmaceutical industry. We continue to work in close cooperation with our customers to ensure that our tailored solutions are safe, effective and suitable for current Good Manufacturing Practice (cGMP).

### Controlled nucleation

The challenge for successful lyophilisation lies in controlling the nucleation temperature (the temperature at which a biological vial freezes). This is the most effective way to producing a homogenous structure within the product.

Lack of control can adversely affect the product’s uniformity due to suboptimal freeze-drying cycles. With our proprietary nucleation technology, liquid nitrogen creates a sterile ice fog that is distributed inside the lyophiliser to simultaneously and uniformly nucleate all of the vials. The uniformity provided by our nucleation technology results in a wide range of benefits, including cycle time reduction, controlled process repeatability, improved product quality and shorter reconstitution time. This technology is applicable to laboratory, pilot and production-scale freeze dryers with the added bonus of eliminating the need for pressure rating.

### Cryogenic lyophilisation

Traditional mechanical cooling systems can be replaced with cryogenic cooling systems, targeting both the shelves and condenser coils. Based on our patented CUMULUS™ design, our cryogenic lyophilisation technology allows pharmaceutical producers to reach significantly lower operating temperatures than those previously possible with industry-standard silicone oil heat transfer fluids. It also enables operators to ramp down temperatures at unprecedented rates. In addition to providing a reliable source of cooling, our solution eliminates the maintenance effort associated with compressors. And it integrates seamlessly into existing lyophilisers with its compact footprint.

Biological products like proteins, vaccines and other injectables must remain effective from manufacture to patient administration. These substances are expensive and fragile, and can easily lose their efficacy during storage.

Valuable biologicals can, however, be stabilised by dehydrating them. This pharmaceutical freeze-drying process is referred to as lyophilisation, and is carried out in highly controlled environments in compliance with increasingly strict regulatory guidelines. Successful lyophilisation extends shelf life and prevents many biopharmaceuticals from degrading.

Our cryogenic nitrogen-based innovations, commercialised in partnership with IMA Life, are being used to enhance various aspects of lyophilisation. They help improve process controllability, flexibility and product quality while reducing costs.

**Our long-standing partner to the pharmaceutical industry.**

Delivering innovations tailored to evolving market needs.

For more information, visit our website at [www.ourwebsite.com](http://www.ourwebsite.com). Contact us today to learn how we can help optimise your process.
Processing innovations for ozonolysis, inerting, purging, charging and mixing. Maximising process safety and quality.

Safe and cost-effective ozonolysis

Ozonolysis is a chemical oxidation reaction using ozone, which is more reactive than oxygen. The use of ozonolysis has been limited to date due to safety and cost concerns. Our innovative approach to ozone recycling in ozonolysis production not only reduces oxygen consumption by over 50% and overall cost of ownership by up to 75%, but also enables ozone to be supplied in either dry air or inert nitrogen. The use of nitrogen increases ozone supply safety for ozonolysis applications.

Inerting and purging with confidence

Often vessels and piping contain gas residue that may be sensitive to atmospheric oxygen exposure. In these cases, it is necessary to limit or remove this exposure in order to prevent explosions, eliminate undesired reactions, keep moisture away from sensitive products and ensure safety during maintenance. This cannot always be achieved through technology and equipment design alone, so inert gases, usually nitrogen, may be used. Inerting can help storage tanks meet safety standards, as well as maintaining and improving product quality. Blanketing, purging and sparging are all forms of inerting that can be applied to pharmaceutical products in storage tanks. Our engineers have vast expertise in the design and delivery of safe, effective inerting systems using our proprietary software.

Safe charging of bulk solids

If air or oxygen enters a vessel during manual charging of bulk solids, this can result in product quality issues and, more importantly, safety hazards. Our patented N2LOCK™ system is an inert gas lock effective in reducing the quantity of atmospheric oxygen admitted when vessels are opened and manually charged. It thus helps to avoid the formation of ignitable mixtures.

Inert vessel mixing

We can provide nitrogen-based vessel mixing solutions to replace mechanical mixers and overcome the disadvantages associated with manual systems. Using a series of accumulator plates attached to the bottom of a variety of storage vessels, gas is injected, causing large, thin bubbles to form and rise to the surface. The customised result for each vessel is faster mixing and better energy efficiency. In addition, operators can control many vessels from a single control panel. Often, nitrogen is the best choice of gas to promote mixing, since it also acts as an inerting agent and will not affect the quality of the product stored in the tank. This technology is ideal for low-shear mixing applications and works well even on high-viscosity fluids.

Cryogenic storage and transport

Cryopreservation with liquid nitrogen allows products and samples to be stored below critical temperature. This means that biological material can be stored almost indefinitely, since the rate of decomposition is extremely low. We offer a range of freezers and containers of all sizes, engineered to maintain specific temperatures between -150°C and -196°C, depending on whether the sample is stored in liquid or vapour phase. To support the transport of frozen microscopic specimens, biological matter and medicine, we provide dedicated storage, dispensing, packaging and transportation services – all designed to ensure strict temperature control.

Freezing

We can supply customised systems for freezing a variety of products such as vials, tablets and blister packages. Liquid nitrogen and liquid carbon dioxide are both versatile cooling agents. Excellent heat transfer is achieved through direct contact between the cryogenic refrigerant and the product. Our freezer systems ensure high-speed freezing for better product quality. Other benefits include a high degree of reliability, simple operation and minimal space requirements. You can pre-test the system of your choice at one of our technology centres.
Gases and supply concepts to suit your every process need. Tailor-made, tested and traceable.

Whatever your gas consumption needs, we can help you find the perfect supply solution. Our scope extends from single cylinders to extensive on-site gas production plants. We have developed traceable gas concepts to help manufacturers comply with applicable GMP regulations. The use of these traceable gases, which have been tested to comply with pharmacopoeia monographs, is a reliable way to increase safety in the manufacturing of pharmaceuticals or APIs.

Our HiQ™ specialty gas concept is designed to meet the needs of the pharmaceutical and API industries. Our HiQ programme includes pure and mixed gases along with the enabling gas equipment and services, backed by dedicated production facilities, accredited analytical laboratories and mobile analytical services. Needless to say, all gas products are quality controlled and, wherever applicable, carry a Certificate of Analysis. We make it our business to ensure that the gas or mixture that you use in your business is the best one for the job.

Specialty gas mixtures and standards for calibration

As a global leader in specialty gas mixtures and standards for calibration, we offer standardised and custom gas mixtures. All mixtures can be designed to meet individual needs for calibrating gas monitoring equipment such as direct read analysers, gas chromatographs, HPLC and threshold monitors. We have many ISO 17025 accredited laboratories across a wide range of countries. In 2009, we earned accreditation as a producer of reference materials to ISO Guide 34 in Europe and Asia, and in 2013 accreditation followed in the United States. We are even certified as a Guinness World Record holder for producing a 110-component specialty gas mixture for calibrating VOC detection equipment. We continue to set standards for the calibration of gas measuring instruments.

Process chemicals – from lab to production

In addition to our standard assortment of industrial gases, we supply a range of gases particularly tailored to the pharmaceutical industry under our HiQ specialty gas programme. These products can be used throughout the entire process chain, from the lab bench through process optimisation in the pilot plant to the full production line. Typical applications and products are:

- Amination: ammonia (NH₃), mono-, di- and trimethylamine
- Bromination: hydrogen bromide (HBr)
- Catalysis: boron trichloride (BCl₃), boron trifluoride (BF₃)
- Chlorination: hydrogen chloride (HCl), chlorine (Cl₂), silicon tetrachloride (SiCl₄)
- Fluorination: hydrogen fluoride (HF), nitrogen trifluoride (NF₃), sulfur tetrafluoride (SF₄)
- General chemical: carbon dioxide (CO₂), sulfur dioxide (SO₂), ethylene oxide (C₂H₄O), hydrocarbons
- Insulation: sulfur hexafluoride (SF₆)
- Methylation: methyl bromide (CH₃Br), methyl chloride (CH₃Cl)
- Phosgenation: carbon monoxide (CO), chlorine (Cl₂)
- Reduction: hydrogen (H₂), diborane (B₂H₆)
- Refrigeration: halocarbons, ammonia (NH₃)
- Thiolation: hydrogen sulfide (H₂S), carbonyl sulfide (COS)
Minimising your environmental footprint. Sustainable solutions for emissions and wastewater management.

Companies today strive to become more sustainable in response to rising environmental awareness among consumers and increasingly strict regulations. The pharmaceutical industry is challenged to minimize releases from manufacturing sites which could impact the environment and human health. Our broad range of environmental solutions can help you meet today’s and tomorrow’s environmental standards.

Wastewater treatment

We commonly supply oxygen and/or ozone to biological wastewater treatment plants to improve aerobic activity, which reduces dissolved oxygen (DO) levels and unpleasant odours. Oxygen can also prevent the formation of hydrogen sulfide in buffer tanks, lagoon piping and sewerage systems. Where standard biological treatment is not applicable, we can offer solutions employing wet oxidation.

We also provide pH control services using carbon dioxide. When dissolved in water, carbon dioxide forms carbonic acid and reduces the pH value to the appropriate level. This process is an attractive alternative to hazardous chemicals such as sulfuric or hydrochloric acids. Not only does it improve safety, it also offers better control.

Volatile organic compound (VOC) emission control

Solvents are commonly used in API manufacturing. Operators must take care not to unwittingly release VOCs to the atmosphere. In addition to regulatory compliance, cost is another driver for VOC recovery. Evaporation losses can prove extremely expensive. Cryogenic condensation of VOCs with liquid nitrogen is an ideal solution for VOC recovery, efficiently condensing VOCs from the waste gas stream and allowing them to be easily captured and routed back into the process or further treated. The resulting gaseous-phase nitrogen can be used for other applications such as inerting. Our well-established, cost-effective CIRRUS® product line supports VOC removal to ppm levels.

Thermal oxidisers for waste disposal and product recovery

We offer proven solutions for the safe and economical thermal treatment of gaseous and liquid waste streams. These versatile, integrated waste combustor systems make full use of the energy contained in high organic waste streams. Organic destruction efficiencies in excess of 99.99% are proven and guaranteed, and valuable by-products and energy can frequently be recovered from the waste streams. Two thermal oxidation options include competitive flame-based units and our exclusive THERMAFIRE™ flameless thermal oxidiser (FTO). Our FTO technology reliably and cost-effectively treats VOCs in flue streams and repeatedly demonstrates 99.99%+ waste destruction efficiency, with NOx and CO emission control that far exceeds flame-based oxidisers.

NOx emissions control

NOx and other pollutants from combustion waste gas streams can be removed with our innovative LoTOx™ technology. This low-temperature, end-of-pipe solution uses ozone to oxidize insoluble NO and NO2 to N2O5 (a highly soluble species of NOx), which can be effectively removed by conventional air pollution control (APC) equipment. LoTOx can be configured for efficiency levels between 30% and 95%+ and can be used as a stand-alone treatment system or as a polishing system in conjunction with combustion modifications or other post-combustion technologies for NOx removal.

Approved quality in gas distribution systems. Perfect fit for your purity and performance needs.

Gas distribution systems

Regulatory agencies rigorously check all relevant documentation to ensure that facilities comply with current regulations. All utilities that might have an impact on product quality – such as steam, gases, heating, ventilation, etc. – should be qualified and monitored. Gas system qualification includes installation qualification (IQ), operational qualification (OQ) and performance qualification (PQ). Gas samples are taken during OQ and PQ and then analysed according to agreed specifications, which in most cases will be those laid down in the pharmacopoeia monographs. We offer a wide range of gas distribution system installations, including:

- Industrial installations
- Specialty gas installations (laboratories)
- Specialty gas installations (cGMP production)
- Ultra-high-purity installations
- Healthcare installations

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Safety, training, services ... and more. Supporting all your gas management and handling needs.

Handling industrial gases requires caution. We provide a range of technologies for improved safety, supporting them with hands-on training in the safe handling and storage of gases. We complement our offering with various gas management services so you are free to focus on your core business. You can even rely on us for testing and analysis services.

Safety first
Safety is a core value within our company culture. Safety is always given top priority in any gas or technology installation. We take preventative action to minimise any risks posed by potentially hazardous gases, gas supply systems, collection processes or disposal. We offer extensive security and maintenance services and can also, in some areas, offer qualified on-site personnel and the reassurance of an emergency response team.

Testing
Various testing facilities are available for our Linde technologies under your conditions. If we supply equipment as part of our solution, Factory Acceptance Tests (FAT) and Site Acceptance Tests (SAT) are also available.

Education and training
We can advise and assist in the development, implementation, control and follow-up of appropriate safety measures and procedures, such as enhancing awareness and training staff. Education and training in applicable processes is considered by cGMP to be of utmost importance. We can assist you in your educational requirements around gases and gas-related process solutions.

Sampling and analysing
To verify the contents of gas systems at factories operating under cGMP requirements, a complete gas analysis should be carried out at least once a year. Through our analytical services, we regularly take gas samples from your factory’s gas system and analyse them in accordance with appropriate regulations.

Cylinder tracking
Thanks to our sophisticated logistics and management systems, we are able to provide cylinder tracking and follow-up services through our dedicated Customer Service Centre.

Total gas management
Our total gas management solution allows you to focus on your core business by linking after all gas management tasks. Total gas management spans everything from inventory control to remote monitoring and includes automatic ordering, cylinder replacement and incoming inspections.
BOC – turning ideas into solutions

BOC is a member of The Linde Group, the leading global gases and engineering company. BOC is the UK’s largest provider of industrial, specialist and medical gases, as well as related products and services. As a leader in the application of technology, we are constantly looking for new ways to provide our customers with high quality products and innovative solutions.

At BOC we help our customers to create added value, clearly discernible competitive advantage and greater profitability. To achieve this we have a comprehensive range of products and services, and technical support which can be customised to meet the individual requirements of our clients.

To keep ahead of the competition in today’s market, you need a partner for whom quality, service, process and productivity optimisation are an integral part of customer support. We are there for you and with you, helping to build your success.

BOC – world-leading knowledge and resources adapted to local requirements.