Pharmaline
Gases for the pharmaceutical industry

Three Gases for Life are hiding in this pharmacy. And immediate reliable protection.
Messer manufactures and supplies gases for the pharmaceutical industry. **Gases for Life** may be invisible, but they have no reason to hide away. For example, medicinal products are rendered inert and packaged in a controlled atmosphere with the aid of nitrogen ($N_2$) or argon (Ar). The production of drugs in powder form involves the use of carbon dioxide ($CO_2$).

**Pharmaline – specially tested gases**

Gases that are used as process aids or inactive ingredients in the pharmaceutical industry must always through their use preserve the quality of the medicinal product.

This results also from EU Directive 2001/83. It obliges the holders of manufacturing authorizations to use only such excipients for medicinal products for which appropriate good manufacturing practice was applied. Furthermore, the holder of a manufacturing authorization is required to verify the authenticity and quality of the excipients.

The Good Manufacturing Practice (GMP) Part II guidelines also attach importance to testing. However the processing aids do not need to be tested if the manufacturer’s Certificate of Analysis is obtained, showing that these raw materials are conform to established specifications.

The use of process gases that have been specially developed for use in pharmaceutical production, and which satisfy the relevant requirements, can therefore reduce the amount of testing that has to be performed by the user.

**In line with the latest guidelines and standards**

In contrast to medicinal products and active substances, there are no binding GMP guidelines for process gases. Messer therefore leans production of its Pharmaline gases on the latest IPEC¹ guidelines and EXCiPACT™² standards. Based on these guidelines and standards, we operate a quality management system that takes account of the specific features of the process gases.

**Quality management without compromise**

The Pharmaline quality management system ensures that our gases reliably fulfil the relevant specifications of the European Pharmacopoeia. Pharmaline gases are batch-managed, controlled, fully traceable and are supplied with a certificate.

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Advantages through know-how transfer
The development of Pharmaline is continuously informed by Messer’s experience with other industries which also have statutory requirements regarding the quality of gases and quality management. For example, this applies to the manufacture of food gases in accordance with ISO 22000, of medicinal gases in accordance with GMP or of medical devices in accordance with ISO 13485.

Rapid response to changes
Messer is focused on process gases. This allows us to identify quickly new requirements and provide our customers with appropriate support. We monitor developments and adjust our Pharmaline manufacture processes and products to the changing specifications and requirements.

Messer has pooled its process gases for the pharmaceutical industry under the name Pharmaline. The gases concerned are argon, carbon dioxide and nitrogen.

**Argon** is a colourless and odourless noble gas that is non-toxic. Argon’s most important chemical property is its inertness.

**Carbon dioxide** is a colourless, non-combustible, odourless and tasteless gas. The special properties of CO\(_2\) include its inertness as well as its high water solubility.

At ambient temperature, **nitrogen** is a colourless, odourless and tasteless gas that is non-toxic. Nitrogen is used as a coolant or as an inert gas. After use, it is returned to the atmosphere unchanged.

The Pharmaline programme makes it easier for manufacturers of medicinal products to comply with the obligations defined in the EU Directive 2001/83 and the GMP guidelines.
Focus on product quality
The Pharmaline quality management system is based on the requirements of ISO 9001, which also form the basis of the EXCiPACT™ standards.

Risk-based approach to manufacture
Design, planning and implementation of our production and control processes are based on risk analysis. This means identifying, analysing and evaluating the specific risks for Pharmaline gases and, on this basis, deriving necessary quality assurance measures.

Manufacture in traceable batches
Pharmaline gases are manufactured in batches. Each cylinder and each cylinder bundle is supplied with a Certificate of Conformity. Bulk gases that are delivered by road tanker are accompanied by a Certificate of Analysis with details on the specifications and the results of the batch analysis. The certificates comply with the recommendations of the IPEC. Records of the entire manufacture process facilitate full traceability of all Pharmaline products.

Tamper-evident seals for quality assurance
Cylinders and bundles in which Pharmaline gases are delivered have a tamper-evident seal, mostly specially developed by Messer. It is an immediate indication that the cylinder in question has remained intact and unopened since it was filled.

Uniform quality
All our Pharmaline manufacturing sites use the same quality management system. If certain process steps are outsourced to external partners, this is done on the basis of clear contractual arrangements. The responsibilities for quality and control measures are defined in the form of arrangements on the demarcation of responsibility.

Continuous monitoring and optimization
Our quality management is subject to continuous monitoring. This includes audits carried out locally as well as centrally. At the same time, we use every opportunity to make improvements. To this end, we promote internal dialogue with regard to the objectives, efficiency, effectiveness and implementation of our quality management. Potential improvements identified in this way are implemented immediately.
### Overview of Pharmaline gases

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| Pharmaline A      | Argon          | Cylinder, cylinder bundle| Ar ≥ 99.999 % by vol. 
Impurities: 
H₂O ≤ 3 ppmv
O₂ ≤ 2 ppmv
Other impurities: 
(N₂, CH₄) ≤ 5 ppmv | Certificate of Conformity |
| Pharmaline A      | Argon          | Road Tanker             | Ar ≥ 99.999 % by vol. 
Impurities: 
H₂O ≤ 3 ppmv
O₂ ≤ 2 ppmv
Other impurities: 
(N₂, CH₄) ≤ 5 ppmv | Certificate of Analysis |
| Pharmaline N      | Nitrogen       | Cylinder, cylinder bundle| N₂ ≥ 99.999 (incl. noble gases) % by vol. 
Impurities: 
H₂O ≤ 3 ppmv 
CO ≤ 5 ppmv 
CO₂ ≤ 3 ppmv 
O₂ ≤ 3 ppmv | Certificate of Conformity |
| Pharmaline N      | Nitrogen       | Road Tanker             | N₂ ≥ 99.999 (incl. noble gases) % by vol. 
Impurities: 
H₂O ≤ 3 ppmv 
CO ≤ 5 ppmv 
CO₂ ≤ 3 ppmv 
O₂ ≤ 3 ppmv | Certificate of Analysis |
| Pharmaline C      | Carbon dioxide | Cylinder, cylinder bundle| CO₂ ≥ 99.5 % by vol. 
Impurities: 
H₂O ≤ 67 ppmv 
CO ≤ 5 ppmv 
NO + NO₂ ≤ 2 ppmv 
Total sulphur ≤ 1 ppmv | Certificate of Conformity |
| Pharmaline C      | Carbon dioxide | Road Tanker             | CO₂ ≥ 99.5 % by vol. 
Impurities: 
H₂O ≤ 67 ppmv 
CO ≤ 5 ppmv 
NO + NO₂ ≤ 2 ppmv 
Total sulphur ≤ 1 ppmv | Certificate of Analysis |

* Nitrogen and argon specifications are higher than the relevant specifications given in the European Pharmacopoeia; carbon dioxide specification is equal to this specification.
Consistent quality from raw

**Application know-how included**
Pharmaline products are as diverse as their applications in the pharmaceutical industry. This applies to product-relevant processes where the gas comes into direct contact with the product, as well as to product-accompanying processes and peripheral processes:

- **Freeze-drying** with liquid nitrogen with the LIN Cryodry® process, in which substances are dried gently in a frozen state under vacuum in order to preserve their biological or chemical properties
- **Powder production** by means of spray crystallization with Variosol®, a process in which liquid carbon dioxide is used to convert a liquid or paste-like product into a free-flowing powder
- **Cold grinding** of starting products with nitrogen or carbon dioxide, because further processing or the use of solid materials often requires fine powders with a large specific surface area
- **Cooling of biopharmaceutical products** with dry ice
- **Cooling of chemical reactors** (Cryocontrol® process) with nitrogen, because many processes used in the production of modern pharmaceuticals and chemicals work at very low temperatures.
- **Inerting** of vessels and supply lines with gaseous nitrogen or carbon dioxide
- **Cleaning** with dry ice
- **Waste air purification** with DuoCondex with nitrogen, for the purification of small to medium-sized waste air flows with high solvent loads
- **Biological wastewater treatment** with oxygen with the BIOX®-N process for predenitrification as well as for simultaneous or intermittent operation of activated sludge basins
- **Neutralization of alkaline wastewater** with carbon dioxide as an environmentally compatible, safe and cost-effective alternative to conventional mineral acids.

**More than gases**
Besides Pharmaline gases, we can also supply you with the necessary equipment or gas supply systems. Where the demand for gases is great, it may make sense to install an on-site facility for the production of gases. Our experts will gladly advise you on these issues.
All Pharmaline gases are delivered with IPEC-compliant certificates.

Each cylinder is given a batch label for clear traceability.

The gases are delivered in cylinders, cylinder bundles or by road tankers as appropriate.

material to certificate

Our equipment and services complete the offering on site.
What Pharmaline offers

- Quality management based on ISO 9001 and leant on the EXCiPACT™ standards
- Product specifications in conformity with the specifications of the European Pharmacopoeia
- Risk-based approach
- Manufacture in batches
- Tamper-evident seals for greater product safety
- Full traceability of all product batches
- Continuous monitoring and optimization of quality management and products

Contact us
If you have any questions regarding Pharmaline or would like to arrange a personal consultation with our application experts, please do not hesitate to contact us.

This brochure and many others can also be downloaded as PDF file from our website: www.messergroup.com