BEKO TECHNOLOGIES

Whitepaper Compressed Air in the Pharmaceutical Industry

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Content

Compressed air – an important component in many processes

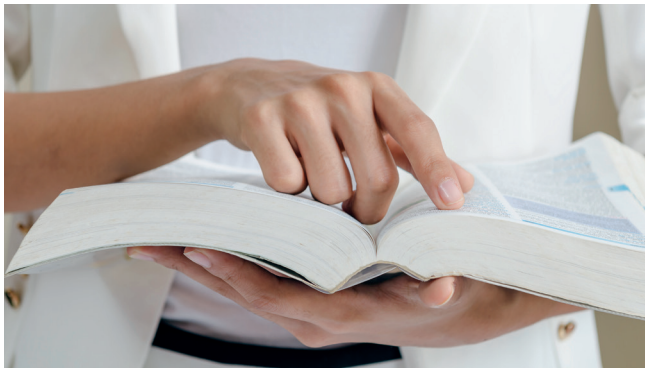
The production of medicinal products without constant compressed air supply is barely conceivable. The medium compressed air is used at many points in the production process, during tablet production, for example, cleaning plants and containers, transporting components or at packaging systems. For these reasons, production companies in the pharmaceutical industry should pay special attention to the medium compressed air in their quality management.

This whitepaper provides an insight into the topic of compressed air in the pharmaceutical industry. It deals with guidelines and laws, the quality of compressed air as well as possible impurities and their sources. Practical examples will also be used to demonstrate why systematic compressed air treatment and seamless monitoring of compressed air are essential for process reliability in pharmaceutical manufacturing.

Which compressed air quality is necessary for a safe production process?

The greatest challenge to compressed air quality management is that there are no concrete legal regulations for the quality of compressed air. Requirements concerning perfect quality and harmlessness only exist for the medicinal product itself. For this reason, pharmaceutical companies must define for themselves which compressed air quality they require for their own process. It is the responsibility of the manufacturer to guarantee the quality of the final product.

An exception to this general rule is so-called aer medicinalis – compressed air which is mainly used as a medicinal production for ventilation and aerosol therapy and in anaesthetics. International laws and standards such as the European Pharmacopeia and the United States Pharmacopeia (USP) regulate this. Both of them define the quality of the air and its regular monitoring.



Good Manufacturing Practice (GMP)

To produce a safe medicinal product, the medium compressed air and thus the entire compressed air plant must be taken into consideration, since this represents a potential risk to the quality of the final product. This is always obligatory for companies producing according to GMP rules (“Good Manufacturing Practice”).

The reason is simple: the GMP are in place to ensure that medicinal products are of a consistently high quality in order to guarantee maximum consumer protection. Concrete specifications are not made, rather instruments are provided to foresee all possible situations. This includes preventative maintenance, for example. One of the core elements of GMP is complete documentation, which also applies for all compressed air-related issues.

Quality requirements depending on the application

For the special case of clean rooms, the requirements for compressed air quality are clearly defined. Compressed air can occur in all cleanroom classes and, according to the FDA Guide for Industry, must at least correspond to the quality of the ambient air into which it escapes. The requirements for cleanroom classes A, B, C and D can be found in the GMP guideline Appendix 1 “Sterile Manufacturing“.

For compressed air applications outside the clean room, the quality requirements are less clearly defined.

A reference point for the selection of compressed air quality to match the respective process is the following categorisation of applications with their different requirements on compressed air (see page 7).
One decisive factor is whether the compressed air is in direct or indirect contact with the product.

High requirements

Low requirements

COMPRESSED AIR TYPE	APPLICATION EXAMPLES	DESCRIPTION
Medicinal compressed air/ breathing air	» Ventilation of patients using compressed air » Aerosol therapy	Compressed air used on patients with a physiological and pharmacological effect. In this case, compressed air is a medicinal product and requires authorisation.
Process air and conveying air for the pharmaceutical industry	» Transport of medicinal products and their components such as powders » Compressed air for loosening up bulk goods » Compressed air at spray nozzles » Compressed air in CIP cleaning » Compressed air for packaging » Compressed air in bio-technological processes » Compressed air for analysis technology	The compressed air is either a constituent part of the medicinal product (excipient) or in direct/ indirect contact with the product.
Control air/ general technical compressed air	» Compressed air for controlling and regulating production lines » Compressed air for blowing particle contamination off workpieces » Compressed air for cleaning particle filters	Compressed air that does not come into contact with the final product

DIN-ISO standard 8573-1

The ISO 8573 series of standards deals with the subject of compressed air quality in nine parts. Parts two to nine cover test methods. Part 8573-1 classifies compressed air on the basis of the maximum permitted contamination content (particles, water and oil).

The standard DIN ISO 8573-1 defines the quality classes of the compressed air with regard to:

Particle size and density

Specification of size and concentration of the solid particles that may still be contained in the compressed air.

Pressure dew point/humidity content

Determination of the temperature at which water vapour condenses to water at the current operating pressure.

Oil content

Specification of the residual amount of oil aerosols and hydrocarbons that may be contained in the compressed air.

The table on page 9 shows the limit values of the individual compressed air classes for the three categories as well as the products, that provide the right compressed air treatment.

› **In order to establish more transparency and safety, the German Mechanical Engineering Industry Association (VDMA) has drawn up the VDMA Standard Sheet 15390.**
It describes in detail which typical quality classes are recommended by VDMA for the different compressed air applications. The compressed air quality classes in accordance with ISO 8573-1 are used. This standard is intended to support users with definition of their requirements and selection of the treatment components.

Class	Solid particles, maximum number of particles per m³			Pressure dew point	Oil content (liquid, aerosol, oil vapour)
	0,1 µm < d ≤ 0,5 µm	0,5 µm < d ≤ 1,0 µm	1,0 µm < d ≤ 5,0 µm	°C	mg/m³
0	In accordance with the device operator's or supplier's specification, stricter requirements than class 1				
1	≤ 20.000	≤ 400	≤ 10	≤ -70	≤ 0,01
2	≤ 400.000	≤ 6.000	≤ 100	≤ -40	≤ 0,1
3	–	≤ 90.000	≤ 1.000	≤ -20	≤ 1
4	–	–	≤ 10.000	≤ +3	≤ 5
5	–	–	≤ 100.000	≤ +7	> 5
6	–	–	–	≤ +10	–

Special case: germ-free/sterile

DIN ISO standard 8573-1 does not define any limit values for germs/micro-organisms. However, absolutely germ-free compressed air is extremely important for manufacturing processes in the pharmaceutical industry, because germs and micro-organisms on the medicinal product endanger the health of the consumer. These can also be removed permanently from the compressed air using compressed air treatment technology like sterile filters or catalysis technology.

Which treatment technologies can be used to ensure the respective limit values are met?

- Compressed air filter
- Compressed air dryer
- Activated carbon filter/ adsorber and catalysis technology

How does
compressed air become contaminated?

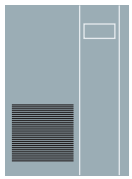
There are many ways for contamination such as particles, oils, germs and humidity to enter the compressed air. They are often already present in the ambient air and get into the compressed air system through the compressor intake air. The reason for the contamination can be a major road or construction site nearby, for example. The risk of humidity occurring in the compressed gas system increases with air humidity in the ambient air.

The contamination presents risks: on the one hand, it presents a real risk to the quality of the final product and thus the consumer, on the other it can impair the function of the compressed air plant and lead to premature wear of plant components.

ENVIRONMENT

Additional hazards exist depending on the direct surroundings and individual circumstances: in addition to dust and humidity, oil and micro-organisms can also get into the compressed gas system via the ambient air.

COMPRESSOR

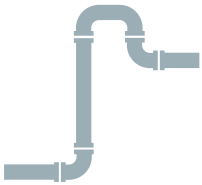


Oil-lubricated compressors can be a source of residual oil vapours in the compressed air system.

VALVES AND FITTINGS

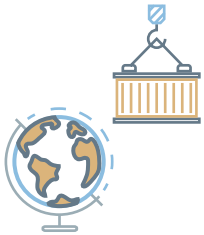
Many components in the compressed air network are lubricated with greases or silicones for better functioning. These substances can easily get into the compressed air.

PIPE



Once a pipe is contaminated, there is a constant risk: over the years, deposits of grease or oil can form in existing pipe networks and can influence the flowing compressed air.

PRELIMINARY SUPPLIER



If the raw materials delivered for manufacturing the product already contain contamination, this can be transferred to the product as well.

Does an oil-free compressor offer air complete safety?

A compressor compressing oil-free does not allow any additional oil to enter the compressed air system. But oil aerosols are already contained in the intake air or can enter the compressed gas system through other components, the compressed air still has to be treated.

Hazard analysis and risk assessment

As described above, all users can specify the exact quality classes in accordance with the DIN ISO Norm 8573-1 standard and consider their individual needs.

However, manufacturers are obliged to document their decision with respect to safety measures within the context of a hazard analysis and risk assessment and to make this transparent. Self-monitoring instruments such as QRM (Quality Risk Management), the HACCP (Hazard Analysis and Critical Control Points) concept and FMEA (Failure Mode and Effects Analysis) provide help with this.

Monitor compressed air quality – but how?

Manufacturers and users of compressed air in the pharmaceutical industry must check which dangers caused by compressed air occur for the medicinal product. Finally, measures must be defined to confine the risk. Monitoring and documentation of compressed air quality at the critical points is vital in order to prove the quality of the compressed air and meet the obligation of proof required for audits and inspections. Alongside quality-related audits for the compressed air itself, the compressed air system is looked at closely during audits concerning energy, the environment and health & safety. Safe compressed air of a consistent quality can only be achieved by compressed air treatment including comprehensive 24/7 monitoring.

Where compressed air treatment is essential

Examples from the pharmaceutical industry

PFIZER MANUFACTURING DEUTSCHLAND GMBH

To improve process reliability in production, the pharmaceutical company Pfizer permanently checks the quality of the compressed air by monitoring the residual oil content using measuring technology and a built-in alarm system. This allows Pfizer to initiate counter-measures before limit values are exceeded. Since the compressed air comes into direct contact with the medicinal product both during coating and blow-off processes at production machinery, the company treats its compressed air in accordance with GMP.

TAKEDA (FORMERLY NYCOMED GROUP)

The pharmaceutical manufacturer Takeda (formerly Nycomed) uses comprehensive system solutions to treat its process air reliably so that it is oil-free. Compressed air is used in numerous processes here: as control air and as an energy carrier for operating pneumatic devices, as an adsorbent following the cleaning of primary packaging materials, for ventilating steriliser chambers and for product superposition in manufacturing. In order to meet the high quality requirements resulting from direct product contact, the company uses both activated carbon filters and an innovative catalysis method which produces compressed air which even exceeds the strict requirements of ISO 8573-1 Class 1.

KLOSTERFRAU BERLIN GMBH

The pharmaceutical company Klosterfrau Berlin GmbH has to rely on stable, dry and oil-free compressed air in its processes. Compressed air is used in the autoclaves in syringe production as well as for syringe filling, and thus has to meet especially high requirements. Alongside compressed air filters, the company uses a heat regenerating adsorption dryer as well as intelligent measuring technology for permanent compressed air monitoring and data logging/documentation.

Intelligent
compressed air treatment requires expertise

Manufacturing companies in the pharmaceutical industry that keep to guidelines such as GMP for their compressed air applications and carry out a hazard analysis and risk assessment have created important pre-requisites for safe compressed air application. Those who monitor their compressed air quality 24/7 are one step further.

In practice, the subject of compressed air is often a critical point for product managers and quality managers. The problem is that the requirements are often not worded clearly in the guidelines, or the effects on the entire plant are not mapped sufficiently. Detailed knowledge is required for the specification of the necessary compressed air quality class and the suitable – i.e. safe and energy-efficient – design of the compressed air treatment.

This is what we can do for you:

Reliable processing, treatment and complete monitoring for flawless results

BEKO TECHNOLOGIES takes the individual requirements of each application into account when designing the compressed air treatment system, thus providing compressed air of the desired quality. So that you can always be sure that the compressed air complies with your requirements and all standards, we make quality measurable and controllable for you.

BEKO TECHNOLOGIES is a manufacturer of system solutions for compressed air treatment and management. We offer safe solutions for stable production processes. Thanks to years of manufacturer expertise and our specialist branch-specific sales, we know the requirements and challenges for your branch very well.

Do you have any further questions about the best way of treating your compressed air?

We have the answers – and suitable solutions for the entire treatment chain. We would be happy to tell you more and present, our condensate processing, filtration, drying, measuring and process technology as well as our comprehensive services.

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