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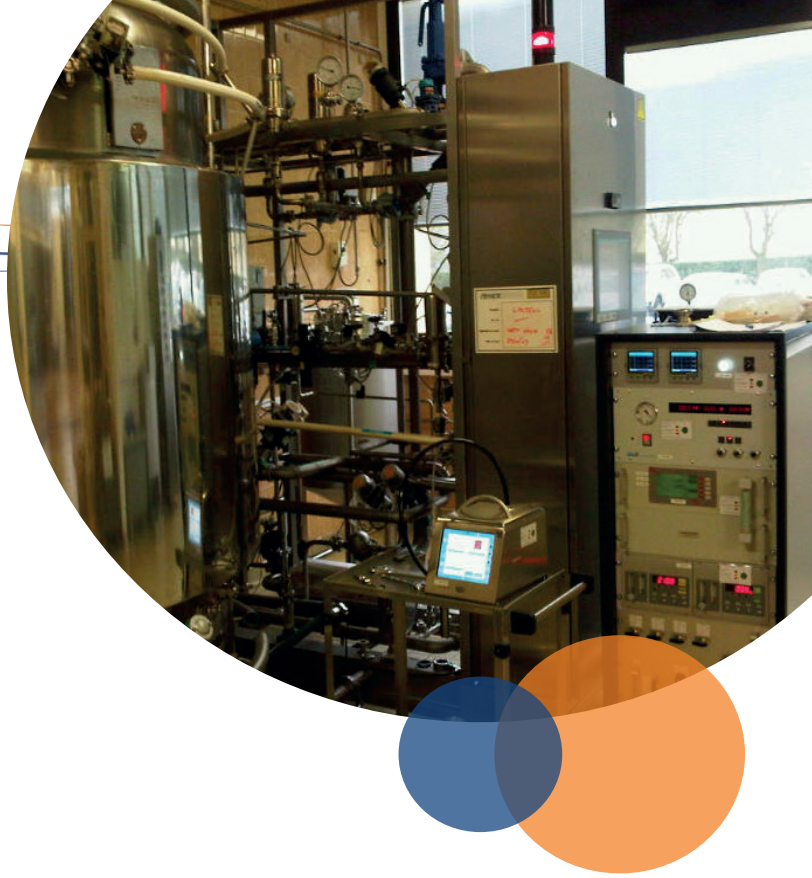
Pharmaceutical Gas Testing



The contamination of classified rooms is a real challenge for the pharmaceutical industry. The fluids used for the production (water, clean steam and vapor of gas) are a potential source of product contamination and cross-contamination from one room to another. The quality of the fluids used should be under control in order to guarantee the quality of the product manufactured on site.

The quality of the pharmaceutical water (purified water or water for injection) is mastered for many years by the pharmaceutical industry and undergoes specific qualification and monitoring plans. Based on this experience, the authorities are focusing now on the quality of pharmaceutical gases. Indeed, gases are used during the production process as an excipient or "invisible helper" in contact of the products such as inerting agent.

Gases that are commonly used in the pharmaceutical industry are:

- Nitrogen for inerting or flushing
- Air for flushing
- Oxygen for fermentation
- Carbon dioxide for extraction and purification

The quality of those gases is specified in the European and U.S. pharmacopeias.

Performing the testing of those gases is a real challenge for the industry since it requires:

- Dedicated analytical equipment according to the pharmacopeias with the appropriate qualification
- Dedicated sampling method fully validated
- Trained and qualified technician with special focus on safety and security issues

In addition, the quality evaluation should be performed at the use point and means access to classified areas.

Besides the pharmacopeias specifications, the gas should also be tested in terms of particular contamination and bio contamination. The contamination of the gas should not be higher than the contamination of the room where it is used. As an example, a gas used in an ISO 5 room, corresponding to the class 100, should be analysed according to the ISO 5 specification in terms of particles contamination.

The specifications for the particular contamination and the bio contamination are reported in tables 1 and 2 on the reverse.

Eurofins has developed the full set of methods with all the dedicated equipment to perform all the tests required for the evaluation of the quality of the gases and the qualification of the pipe works for the pharmaceutical industry.

Table 1: Specification and methods according to the European Pharmacopeia

Gas	Element	Method	Specification
Air	O_2	Ph. Eur. 2.5.27 : Paramagnetic analyser	20,4% - 21,4%
	H_2O	Ph. Eur. 2.5.28 : Electrolytic hygrometer	max. 67 ppm
	Oil	Ph. Eur. 2.1.6 : Impaction	max. 0,1 mg/m³
	CO	Ph. Eur. 2.5.25 : Infra Red analyser	max. 5 ppm
	CO_2	Ph. Eur. 2.5.24 : Infra Red analyser	max. 500 ppm
	SO_2	UV Flurorescence analyser	max. 1 ppm
	NO/NO_2	Ph. Eur. 2.5.26 : Chemiluminescence analyser	max. 2 ppm
Nitrogen	N_2	Ph. Eur. 2.2.28 : GC-TCD with injection loop	min. 99,5%
	H_2O	Ph. Eur. 2.5.28 : Electrolytic hygrometer	max. 67 ppm
	CO	Ph. Eur. 2.5.25 : Infra Red analyser	max. 5 ppm
	CO_2	Ph. Eur. 2.5.24 : Infra Red analyser	max. 300 ppm
	O_2	Electrochemical analyser	max. 50 ppm
Oxygen	O_2	Ph. Eur. 2.5.27 : Paramagnetic analyser	min. 99,5%
	H_2O	Ph. Eur. 2.5.28 : Electrolytic hygrometer	max. 67 ppm
	CO	Ph. Eur. 2.5.25 : Infra Red analyser	max. 5 ppm
	CO_2	Ph. Eur. 2.5.24 : Infra Red analyser	max. 300 ppm
Carbon Dioxyde	CO_2	Ph. Eur. 2.5.24 : Infra Red analyser	min. 99,5%
	H_2O	Ph. Eur. 2.5.28 : Electrolytic hygrometer	max. 67 ppm
	CO	Ph. Eur. 2.2.28 : GC-FID with methaniser	max. 5 ppm
	S	UV Flurorescence after 1000°C oxydation	max. 1 ppm
	NO/NO_2	Ph. Eur. 2.5.26 : Chemiluminescence analyser	max. 2 ppm

Table 2: ISO Clean Room Standard for Particles

EU	US	PARTICLES CLASSIFICATION SCHEME					
CLASSES	ISO	MAXIMUM PARTICLES/M³					
		≥0.1 µm	≥0.2 µm	≥0.3 µm	≥0.5 µm	≥1 µm	≥5 µm
ISO 3	1	1,000	237	102	35	8	NA
ISO 4	10	10,000	2,370	1,020	352	83	NA
ISO 5	100	100,000	23,700	10,200	3,520	832	29
ISO 6	1000	1,000,000	237,000	102,000	35,200	8,320	293
ISO 7	10,000	NA	NA	NA	352,000	83,200	2,930
ISO 8	100,000	NA	NA	NA	3,520,000	832,000	29,300