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BIO/PHARMA - MEDICAL DEVICES - COSMETICS - BIOCIDES

Pharma Services News

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Pharmaceutical gas testing

By Gautier Decock, Eurofins Pharma Control, France

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.

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

Table 1: Specification and methods according to the European Pharmacopeia

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 2 and 3.

EU	US	PARTICLES CLASSIFICATION SCHEME					
CLASSES ISO		MAXIMUM PARTICLES/M³					
		≥0.1 µm	≥0.2 µm	≥0.3 µm	≥0.4 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	1,000	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

Table 2: ISO Clean Room Standard for particles

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.

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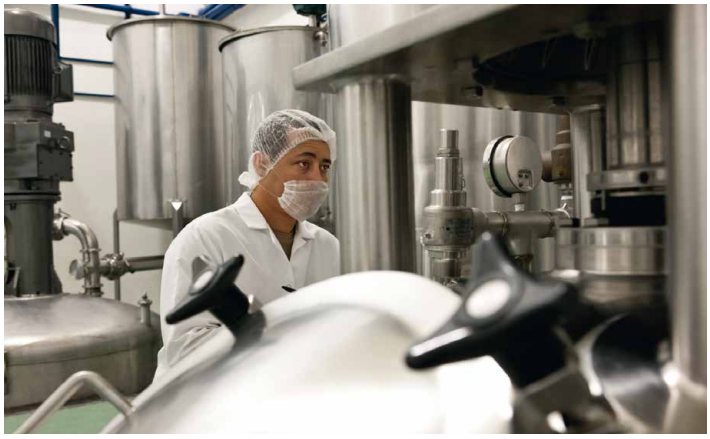
Process contaminants in biopharmaceuticals: Host cell DNA & protein

By Weihong Wang, Ph.D., Eurofins Lancaster Laboratories Molecular and Cell Biology Group, USA, and Philipp Hauri, Eurofins GeneScan, Germany



Biopharmaceuticals such as therapeutic antibodies and recombinant proteins are produced in genetically engineered host cells. Effective removal of host cell contaminants from the production cell lines is required by regulatory agencies to ensure product safety. In general, levels up to 10 ng residual host cell DNA per dose, depending on the host cell type and the route of administration, and 100 ppm for residual host cell protein are acceptable.

To quantify host cell DNA, quantitative real-time PCR offers superior sensitivity with a limit of quantification in the sub-picogram range. Existing PCR systems cover a wide variety of host cell types like *E. coli, P. pastoris*, CHO or human expression systems. Proper performance of the whole analytical procedure, including sample preparation, DNA extraction and PCR analysis is thoroughly verified for each sample matrix before routine testing. If higher specificity of detection is required (e. g. specific detection of the genetically engineered production cell line), Eurofins offers assay development and validation of methods according to customer specifications.

To quantify host cell protein, the ELISA method offers the highest sensitivity and reproducibility. For early phase products, commercially available generic ELISA kits may be used. However, for the testing of late phase or marketed products, an ELISA using antibody raised against process-specific host cell proteins is more desirable. As in all residual testing, sample matrix effects need to be carefully assessed using dilution linearity and spiking studies to ensure the validity of the testing results.

Several laboratories within the Eurofins Group have extensive expertise in method development and GMP testing of process contaminants. For more information, please visit:

- *http://pharm.lancasterlabs.com/biopharmaceutical/molecular_cell_biology*

- *http://www.eurofins.de/food-analysis/analytical-testing/residual-dna-testing.aspx*

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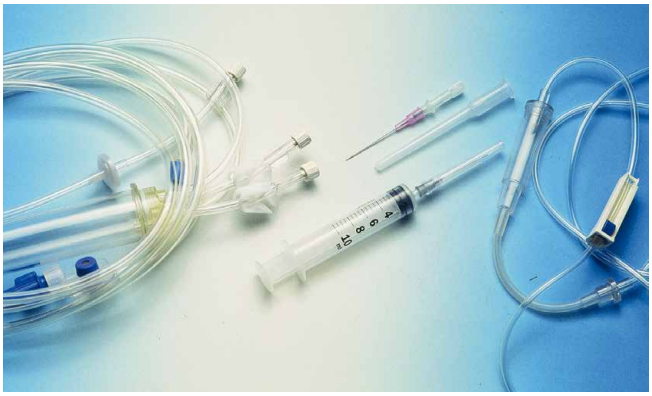
Biological evaluation of medical devices

By Paolo Pescio and Alessandro Radici, Eurofins Biolab, Italy

To date, the medical devices market is one of the most dynamic and active in the world, and everyday many new products are designed and then released to the marketplace. Many of these new products are aimed to be in direct contact with patients; therefore thorough safety assessment of the new devices is a critical step during the design and marketing process.

A medical device is generally defined as any instrument, material, apparatus for humans with a medical purpose and which does not achieve its primary intended action in or on the human body by pharmacological, immunological or metabolic means. Whereas in those cases, it will be a bio/pharmaceutical product.



One of the most relevant requirements each device has to comply with is the compatibility between the materials used and biological tissues. This property is often called biocompatibility, and it is assessed through a biological evaluation process. The biological evaluation of a device is usually based on international standards of the ISO 10993 series, together with different guidelines adopted in different countries around the world.

The biological evaluation is a structured programme in which the choice of tests shall take into account the chemical composition of the materials, including the conditions of exposure as well as the nature, degree, frequency and duration of exposure of the device to the patient.

Eurofins has had the opportunity during the past several years to develop sound experience in biocompatibility testing and can fulfil all the possible analytical needs of a manufacturer while evaluating a device thanks to its accredited world-class labs. Eurofins experts participate in international ISO groups in charge of the development of the standards, enabling scientists to continually be updated and aware of current and future regulatory and technical status pending changes.

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Award-winning Professional Scientific Staffing^{sm} delivers workforce solutions for 10 years

By Beth DiPaolo, Eurofins Lancaster Laboratories, USA

With the global economy in a seemingly endless state of flux, companies continually face greater challenges to juggle the demands of increasing expenses and shrinking budgets. As the bio/pharmaceutical industry seeks to reduce costs, there is a significant trend to not only outsource laboratory services but insource laboratory services. Companies faced with fixed (or reduced) headcounts and variable workloads are collaborating with laboratory services providers to help them solve their workload and staffing challenges.

Eurofins Lancaster Laboratories' award-winning Professional Scientific Staffing (PSS) places full-time scientists and support personnel, directly at the client's facility. Hired, trained and managed by Eurofins Lancaster Laboratories, PSS provides a non-permanent, long-term and cost-effective way to meet in-sourcing service needs, while delivering same scope of services, expertise and cGMP compliance available at Eurofins Lancaster Laboratories' facilities.

Fully compliant with co-employment and EU law, PSS provides the client's laboratory with highly skilled scientists who deliver an extensive range of both scientific and support services, while utilizing the quality systems within the client's facilities. This insourcing approach frees up the client's own employees to address core business priorities, while offering a highly managed and productive, cost-effective, non-temporary workforce solution that doesn't fall under the Temporary Workers Directive in Europe or violate co-employment in the US.

A pharmaceutical company executive and PSS client said, "We had a lot of projects that had to be done very quickly and didn't have the resources to do them. We had extremely tight turnaround times and proprietary methods that needed to remain in-house. Addressing every problem we had, PSS delivered solutions with high-level scientists using our methods in our house faster than outsourcing."

Celebrating 10 years of strategic insourcing partnerships and receiving numerous client supplier awards, PSS has grown over 50 percent for the last four years to include more than 25 global sites with more than 500 employees.

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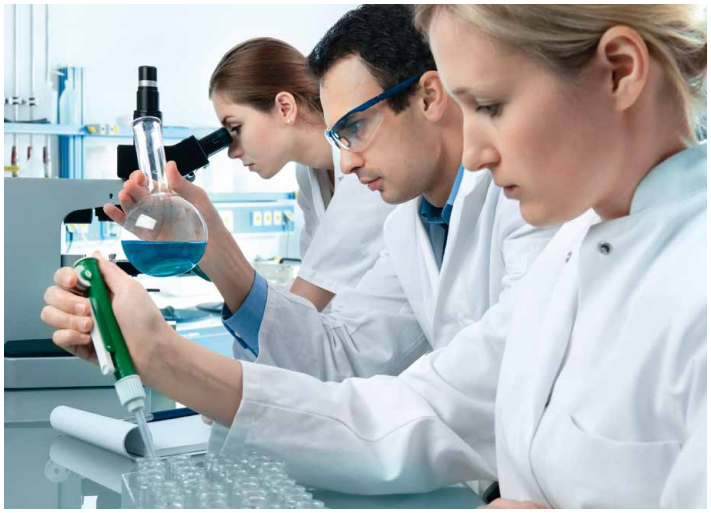
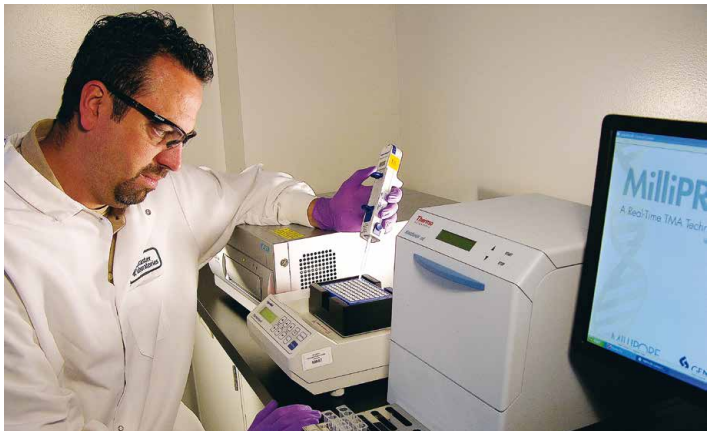


Rapid mycoplasma testing delivers sensitivity, specificity and speed to a broad scope of matrices

By Jeri Ann Boose, Ph.D., Eurofins Lancaster Laboratories, USA



Mycoplasmas are small, self-replicating prokaryotes that are common contaminants of mammalian cell culture. Mycoplasma contamination of cell lines used to produce biopharmaceutical products can disrupt cellular growth and metabolism and lead to changes in gene expression. These adverse cytopathological events can result in decreased product quantity and quality. As mycoplasma infections have been associated with numerous human diseases, world-wide regulatory agencies require that biotechnological products produced in cell substrates be tested to ensure the absence of mycoplasma contamination.

Current compendial mycoplasma testing procedures are 28 days in duration. This time requirement is not amenable for obtaining the rapid lot release testing results needed for biopharmaceutical products that have short half-lives or for which there is high market demand. The 28-day assay time is also not conducive to the rapid screening of raw materials used in production or to the rapid in-process screening of intermediates for the early detection of a mycoplasma contamination event.

Eurofins Lancaster Laboratories now offers the EMD Millipore MilliPROBE® Real Time Detection System for Mycoplasma, a rapid test comparable in sensitivity and specificity to the current 28-day compendial method. In addition to the fact that unaudited data can be sent the same day as testing, other advantages include the fact that the volume of material that can be put on test is comparable to that of the 28-day method and the fact that the method preferentially detects viable mycoplasmas. The system is also less prone to sample matrix effects than other commercially available rapid mycoplasma detection methods.

Eurofins, thanks to recent developments at Eurofins Lancaster Laboratories where they completed validation of the MilliPROBE® System this summer, has begun commercially offering both GMP and non-GMP versions of the assay to its international customers. For more information, visit: *http://pharm.lancasterlabs.com/content/rapid-mycoplasma-testing*.

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Eurofins expands presence in discovery pharmacology with the acquisition of Pan Labs US

Pan Labs, a leading provider in early stage discovery services, offers an unmatched portfolio of more than 1,300 In Vitro and In Vivo pharmacology assays that enable science-driven selection at every stage of the drug discovery and development process. Pan Labs has over 150 highly qualified employees and USD 20m in annual revenues with most of the largest global pharmaceutical companies. Pan Labs' portfolio of services includes molecular and functional pharmacology, cellular services, and informatics analytics. Here is a brief summary of Pan Labs' extensive pharmacology profiling portfolio:

- 310 enzyme assays
- 210 radioligand binding assays
- 120 GPCR assays
- 95 cellular assays
- 110 tissue assays
- 185 in vivo models
- 85 anti-infective assays
- 45 tumor assays
- 252 human cell line assays
- 17 assay packages

For more information, please contact Jamie Baumgartner, PhD, President of Eurofins Pan Labs: *jamiebaumgartner@eurofins.com.*

COMING EVENTS

EVENT	DATE & PLACE	MORE INFO	CONTACT
Pharmaceutical Gas Testing	9.10.2012, Colmar, France	*In French only*	*GMP_EU@eurofins.com*
Medtec Ireland	10.-11.10.2012, Galway, Ireland	*Booth N°306*	*GMP_EU@eurofins.com*
Pharmaceutical Gas Testing	18.10.2012, Paris, France	*In French only*	*GMP_EU@eurofins.com*
AAPS Annual Meeting	14.-18.10.2012, Chicago, USA	*Booth N°3030*	*GMP_EU@eurofins.com*
PDA on Pharm Microbiology	22.-23.10.2012, Bethesda, MD, USA	*Booth N°30*	*GMP_EU@eurofins.com*
A3P congress	23.-25.10.2012, Biarritz, France	*Contact us*	*GMP_EU@eurofins.com*
Well Characterized Biologicals	29.-31.10.2012, Bethesda, MD, USA	*Booth N°2*	*GMP_EU@eurofins.com*
Partnerships in Clinical Trials	6.-9.11.2012, Hamburg, Germany	*Booth N°719*	*clinicaltrials@eurofins.com*
European Bioanalytical Forum	14.-16.11.2012, Barcelona, Spain	*Booth N°B2*	*bioanalysis@eurofins.com*
Clinical Outsourcing 2013	6.-7.2.2013, London, UK	*Contact us*	*clinicaltrials@eurofins.com*
8th Annual Biomarker Congress	19.-20.2.2013, Manchester, UK	*Contact us*	*clinicaltrials@eurofins.com*
New Dynamics of Biomarker Labs	27.-28.2.2013, London, UK	*Contact us*	*clinicaltrials@eurofins.com*

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