Effective Compressed Gas Contamination Monitoring: Particles and Microbials Frequently Asked Questions

This FAQ paper is a follow up to the webinar, "Effective Compressed Gas Contamination Monitoring: Particles and Microbials". Many thoughtful questions were asked about successful compressed gas application, control of particles and microorganisms in pharmaceutical manufacturing and contamination prevention methods. Questions submitted during and after the webinar are answered below. If you have any additional queries for our experts, submit them directly here.

Topics in this paper include:

- **Sampling Methods**
- **Compressed Gas Sampling**
- **ISO 8573**
- **Sterilization and Contamination Risk**

TOPIC: SAMPLING METHODS

What types of media would you recommend for microbial testing?

Compressed gas applications typically use TSA media, or its variations, with neutralizers included. This media is the same as what's used in the viable air monitoring of the room into which the gas is released.

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Why is microbial impaction preferred over membrane filtration?

Microbial methods are targeted towards the recovery of microorganisms. This means that microorganisms must stay alive to grow on the agar media and become visible colonies.

Membrane Filtration methods impose strong mechanical forces and dehydration resulting in lower recovery. For the same reason, the impaction speed of samplers need to be managed carefully.

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What is the advantage of the Impaction (STA) method over the Liquid Impingement method for sampling of compressed air for viable count estimation?

The main advantage is Impaction can handle higher flow rates. There is no easy way to validate the recovery of Liquid Impingement, whereas ISO 14644 gives clear guidance on the validation of air samplers.

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What is the best risk assessment model to assess sampling locations and frequency?

Refer to the ISO 14644-2 recommendations in order to correctly define a defensible and efficient monitoring plan, well supported by a well developed risk assessment. More information on common risk assessment models can be found in the ISO 14644-2 application note and webinar, available here.

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TOPIC: COMPRESSED GAS SAMPLING

Is microbial and particle monitoring required for every batch?

Generally speaking, monitoring is an exercise to keep the quality of compressed gas (CG) under control, and is not a batch related exercise. Monitoring ensures that the measures you have taken (e.g. a sterilizing grade filter) works according to specifications. If a risk assessment reveals that the associated risks of CG towards the product is too high, batch sampling is required, but a more typical approach to ensure quality of the gas would be to do an integrity test of the filter.

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What are the set points for pressure and flow rate that will allow sampling with PMS equipment?

Both minimum gas pressure and sample flow rate are defined by the instrument's specifications. Consideration should be given to sampler selection (either a particle counter or microbial sampler) and the specific High Pressure Diffuser kit specific to your compressed gas line.

Another important parameter is the type of gas to be sampled, which may not be compatible with your sampler.

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What is the limit for microorganisms in CG used for production of non-sterile medicine forms?

Limits on CG are related to the air limits that are used in the environment where the sampling site is located. According to GMP regulations, they must be established based on historical data.

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What is the lowest gas pressure instruments can handle?

The Minicapt® Mobile Microbial Sampler can handle pressure starting from 0.5 bar (7.2 PSI) at 25 LPM.

The Lasair® III Particle Counter can handle pressure starting from 1.7 bar (25 PSI) at 28.3 and 50 LPM.

As part of continuous improvement activities, Particle Measuring Systems will release a specific version of the Lasair III High Pressure Diffuser which will be able to sample lower pressurized gases from 5 PSI.

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Filling line operation with the MiniCapt Mobile and Lasair III

What is the maximum tubing length for gas sampling?

The loss of particles due to deposition in tubing is negligible for compressed gas sampling applications. The high pressure and flow speed conditions, as well as turbulent flow paths in tubing (high Reynolds number) contribute to this.

It is not necessarily negligible when using devices with a decompression stage before the sampling point.

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What is the best compressed air tubing material for viable and non-viable contamination?

Sample tubing used for compressed gas sampling must provide appropriate resistance to air pressure to guarantee safety operations.

Commonly used tubing includes, but is not limited to, the following materials: stainless steel, PTFE, polyurethane, and Tygon®.

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How do you sample gas pressure at < 25 psi? It is handled directly with the Lasair III? Is there an impact on the instrument?

Gas pressure is sampled directly with the Lasair III particle counter, without additional precautions such as a pressure regulator and/or a T-connection which allows excess gas to exit the line, which may result in inaccurate particle sampling due of a possible high flow rate in the optical cell.

The instrument flow regulator is designed to compensate and adjust the sampling flow within certain limits. Refer to the instrument reading and alarm indicators to help avoid inaccurate samples.

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Where in the manufacturing facility should compressed gases be sampled? Is it acceptable to sample above the room (i.e., in the attic) or does it need to be at the point of use?

It is required for the sampling of compressed gas to be done at the point of use, or as close as possible to it.

Sampling performed in another location may not provide any indication about possible line contamination occurring between the sampler and the point of use.

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Does the compressed gas monitoring data need to be stored and trended?

Yes, compressed gas control is one of the many environmental controls required in a cleanroom. ISO 14644-2 requires several measurements be taken to verify cleanroom performance. Data should be stored, trended and analyzed on a yearly base.

Sampling data should reflect data integrity requirements for GMP compliance.

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Why don't accessory kits require calibration?

The compressed gas accessories supplied by Particle Measuring Systems do not require any additional calibration because the sample flow rate is controlled, in real time, by the sampler itself.

During annual calibration, the sampler (Lasair III or Minicapt Mobile) receives an accurate flow calibration in accordance with the current standard, guaranteeing the compressed gas kit will work properly while sampling a compatible gases.

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For total airborne particulate testing of compressed gases such as O_2, N_2,CO_2 and compressed air, can the Lasair III be used? Is it one instrument fits all for PMS particle counters?

The Lasair III can sample air, argon and N_2. For other gases, we recommend the HPGP particle counter.

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High Pressure Gas Probe 101-C

How does dryness of the gas impact false positive counts?

Dry gas can result in a “false count” reading due to possible particle shedding from the optical chamber in when sampling

Typically, very dry gases are measured for a short period of time (e.g. 15-20 minutes) and then allowed to rest before the next sample for about 30 minutes. This method works well with the Lasair III. However, if the sampling is done for more than 20-30 minutes continuously, counts may become unrelated to the gas.

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What is the quantity of compressed gas that needs to be sampled, especially where it is used in Grade A? What are the normal industrial practices?

The sample volume commonly used for compressed gas classification reflects the actual volume used for cleanroom control.

For example, gas used in Grade A cleanrooms are sampled using a 1 cubic meter volume target.

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We use CG sampling to dry production parts. Despite a series of in-line filtration and water traps, the particle counts were still higher than required for food grade CG. What are some common failure modes for this?

First, look at how sampling is done and remove risks of external contaminations (e.g. using agar stripes, touching the agar, working in dirty environments, dead legs and biofilms at sampling ports, etc.). A disinfection of the CG line should be considered, as well as an understanding of risks for condensation in the line associated with water build up. Make sure to maintain an appropriate dew point.

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Can your instrumentation be used to sample oxygen systems or due to safety concerns (i.e. explosion) is it not recommended to sample these systems?

Sampling of oxygen must be done using appropriate and specifically designed instruments, such as the HPGP particle counter. This is for both accuracy and safety concerns.

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TOPIC: ISO 8573

Is ISO 8573 applicable to the pharmaceutical industry?

ISO 8573 is a generic standard for all industries where compressed gas control is required.

Specifically, regulators refer to ISO standards as a source for "state of the art" methods.

ISO 8573 should be strongly considered for the production of compressed gas, while users monitoring the sampling point should refer to the specific GMP standards applicable.

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Do ISO standards allow for pressure reduction?

Yes, both ISO 8573 parts 4 & 7 allows for gas pressure reduction to be performed in accordance with the instrument manufacturer recommendation.

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It seems that intervals specified in ISO 8573 are not suitable for laser particle counters. Response?

You can refer to the differential count reading to evaluate the particle count between the specified channels.

The ISO 8573 is a generic standard for all industries, where the compressed gas control is required. For pharmaceutical gas control, refer to ISO 14644/GMP particle limits, as required by the FDA guidelines.

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ISO 8573 states specifications for particulates, water vapor and oil. Alternatively, CG specs can be set to cleanroom specs. This would depend on the specific process, but are there any references for setting bioburden specs?

There are no specifications for viable air monitoring in CG aside from the link between existing GMP standards for the air into which the compressed gas is introduced.

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What is the basic difference between routine and long term routine monitoring?

Routine monitoring starts when the initial qualification has been performed. Historical data will be generated in the first months of routine testing.

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Regarding non-viable air monitoring, can moisture cause false readings during non-viable air sampling?

Non-viable particle counters are designed for sampling in a wide temperature/humidity range. You should refer to the particle counter specification sheet and avoid condensing gas sampling.

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What is the recommendation for sampling volume? It a cubic meter necessary at every point, or only specified locations?

For classification purposes, it is recommended to sample the compressed gas using the same volume requirements applied for the cleanroom classification where the gas is going to be used.

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TOPIC: STERILIZATION AND CONTAMINATION RISK

For very large systems, what is the strategy for placement of sterilizing filters?

There is definitely a need to put sterilizing grade filters as close as possible to the point of use. Other filters for bioburden/particle reductions should be placed where tubing enters into clean-zones of higher quality in order to protect additional sampling points in these areas.

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Is IPA adequate to disinfect samplers between samples?

Yes, IPA is a good disinfectant solution.

Regarding the microbial compressed gas supplied by Particle Measuring Systems, it can be fully autoclaved for sterilization purposes.

IPA is not sporicidal and in dry compressed gases, spores are considered more relevant. Therefore, a sporicidal agent might be necessary. On the other hand, flushing the equipment with the gas to be sampled might be sufficient to remove contamination of the sampling point and avoid cross-contamination from a previous point. Of course, it all depends on the expected cleanliness of the gas and the resulting issues in case of OOS.

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Do cleaning agents, like 70% IPA, affect machine operation for compressed air monitoring or its calibration?

Disinfection and cleaning of the compressed gas kit can be performed with a wide range of products, including 70% IPA.

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Are the accessories supplied with PMS air samplers autoclavable?

All surfaces in contact with gas are autoclavable.

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Does the treatment of compressed air by heating and filtering in the compressor room minimize the risk of contamination at the point of use?

It surely does, but this effect is hard to validate when assessing the efficiency of these operations.

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What are the risks of using an instrument not equipped with an exhaust HEPA filter?

The major risk of using an instrument without HEPA filtered exhaust is the delivery of a potentially contaminated gas into the cleanroom.

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