Cleanroom Monitoring

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What is monitoring?

Monitoring is the **regular observation** and **recording** of activities taking place in a project or process.

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Why is this important?

The moment a **Cleanroom** is completed, it provides the ability to gain and maintain varying levels of process control by design, however without monitoring this, continued compliance cannot be proved or documented.

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Classification vs. Monitoring

The difference between **classification** and **monitoring** is similar to that of your car MOT and daily operation.

Classification is the annual or bi-annual service routine in which you ensure everything is in its best possible state before presenting it to the tester.

Monitoring is what your dashboard tells you on a daily basis such as speed, fuel levels, warning and action lamps etc.

Cleanrooms are no different.

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So why monitor?

Monitoring within a cleanroom **reduces the risk** of an out-of-specification condition and helps facilities **remain audit-ready** and compliant.

Whereby classification is typically carried out by a third-party, monitoring is performed by the facility owner and is performed much more frequently, if not continuously.

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What can you monitor?

Depending on the application, there are a wide range of parameters which can be monitored which include but are not exclusive to;

- Particulate levels (viable and non-viable)
- Differential Pressures (room pressure and HVAC pressures)
- Temperature
- Relative Humidity and Dew Point
- Static
- Oxygen depletion

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Non-viable particle monitoring

To ensure that your product is manufactured with the facility within the thresholds of its validated state, monitoring particulate levels is imperative. This not only gives feedback on room condition but can help drive process improvements and operator training. This monitoring is often done in the following ways;

Sequential – Performed using a multiplexing system at multiple locations, cycling each location systematically.

Continuous – Performed using one or more remote counters which are operated round the clock.

Periodic – Performed at defined intervals (i.e weekly or process orientated) using a handheld or bench top particle counter.

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Differential Pressure Monitoring

In order to prove both effective zonal segregation and HVAC system operational effectiveness, it is important to monitor differential pressures.

Room Differential Pressures– Measured either ‘room to room’ or ‘ room to atmosphere’ to prove an effective pressure cascade giving effective product and/or personnel protection.

HVAC differential pressures - In order to understand HVAC operation and effectiveness, AHU or fan filter differential pressures can be monitored to give an indicator to motor operation and filter life.

Differential pressure can be monitored mechanically through magnehelic pressure gauges or electronically using a differential pressure sensor, often both if the risk assessment deems this necessary.

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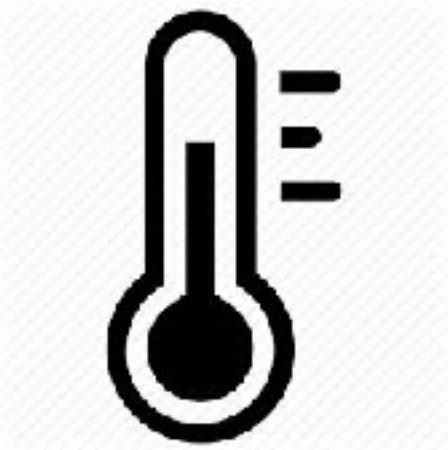
Temperature and Humidity Monitoring

Whether for operator comfort or as a process critical control, monitoring temperature and humidity can help optimise facility effectiveness. Often used to drive the output of HVAC plant and PI control loops, well placed temperature and humidity sensors can reduce energy usage and reduce condition fluctuations.

Where should I monitor?

- Return air – for the best effective HVAC plant control
- Room side – for operator comfort
- On room equipment – for plant control conditions



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Open Loop vs Closed Loop

With energy efficiency an ever growing concern, using monitoring to help reduce energy usage can significantly reduce running costs.

As cleanroom functional design often has many interdependencies, closed loop control can drive and control system outputs.

A good example is using room condition feedback to drive reduced plant output in times of minimal room usage or set back modes.

Alert and Action Limits

With any monitoring system, warning levels need to be in place on performance critical parameters and typically these are done using alert and action limits;

- **Alert Limits** - An early warning level used to prevent an Action limit being reached.
- **Action Limits** – When exceeded, immediate action should be taken with root cause investigation and corrective action.

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What standards are applicable?

- **ISO 14644-2: 2015.** Cleanrooms and associated controlled environments - Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration.
- **EU GMP Annex 1.** The Rules Governing Medicinal Products in the European Union "Cleanroom and clean air device monitoring“.
- **FDA Guidance** for Industry Sterile Drug Products Produced by Aseptic Processing.
- **World Health Organization (WHO)** Environmental Monitoring of Clean Rooms in Vaccine Manufacturing Facilities
- **US FDA, 21 CFR 210 and 211**, Current Good Manufacturing Practice for Finished Pharmaceuticals, details the requirements for cleanrooms needed to assure the integrity of the finished product.

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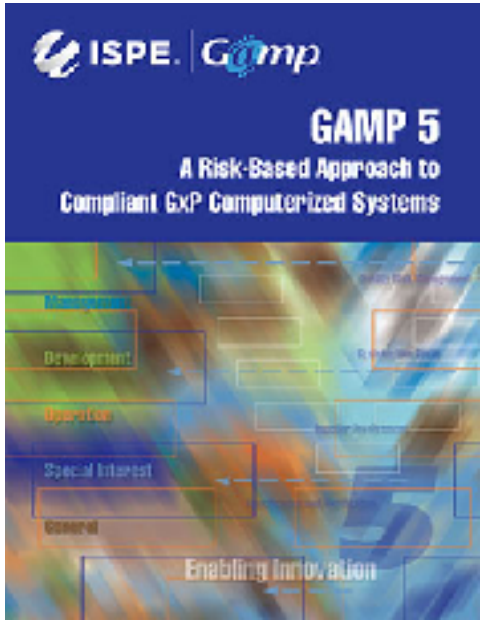
The Approach

In order to ensure that you design or purchase a cleanroom monitoring system that meets your requirements, it is important to take the right approach when specifying and implementing the system.

To assist with this process ISPE published the **GAMP5 guidelines for Compliant GxP Computerized Systems.**



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What type of system do I need?

As there is a plethora of systems and instrumentation available to monitor cleanrooms it is important to know what kind of system to specify. These are generally;

- **Off the shelf systems** – Scalability limitations, fixed functionality, very limited validation required
- **Configured systems –** Scalable system, fixed functionality, minor system validation required
- **Coded/Bespoke Systems –** Scalable system, proprietary functionality can be accommodated, full system validation required.

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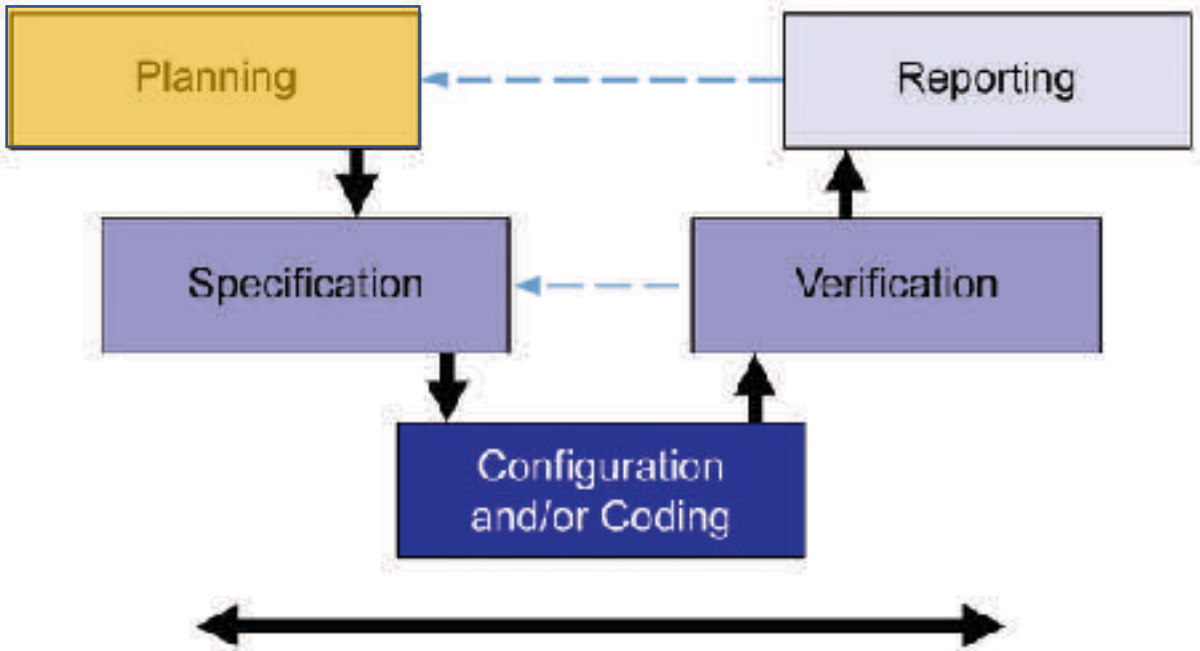
The Approach



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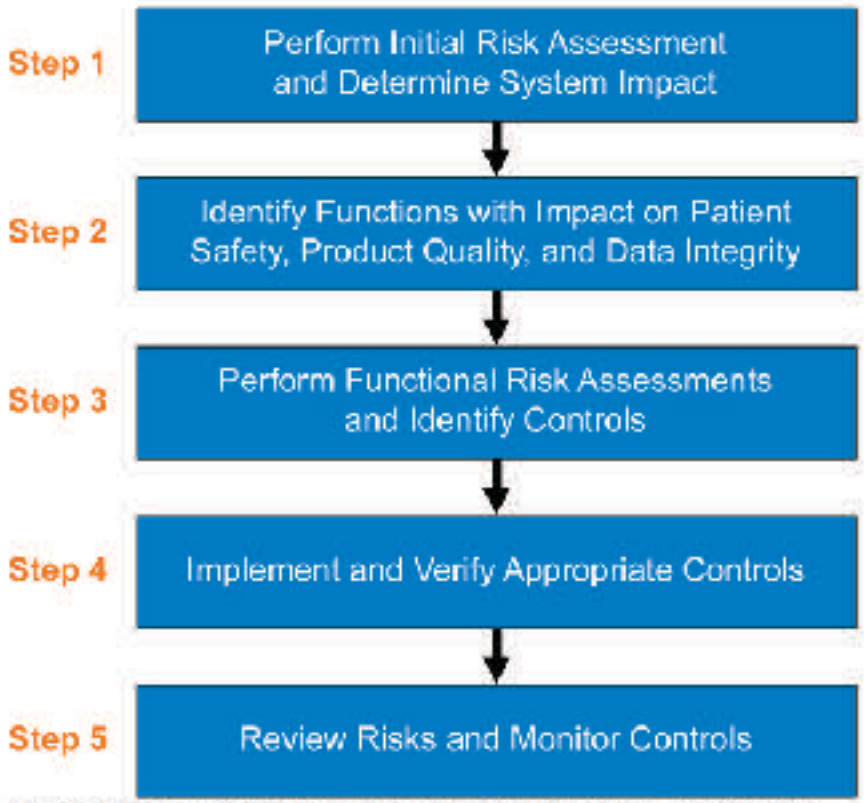
Risk Assessment Process

A risk assessment is the first step to plan and achieve the best monitoring solution.



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What to consider?

- What are the **overall risks** to the business?
- What is the overall **impact of the system**?
- Identify **risks specific to processes**.
- **Define controls** and reduce risk

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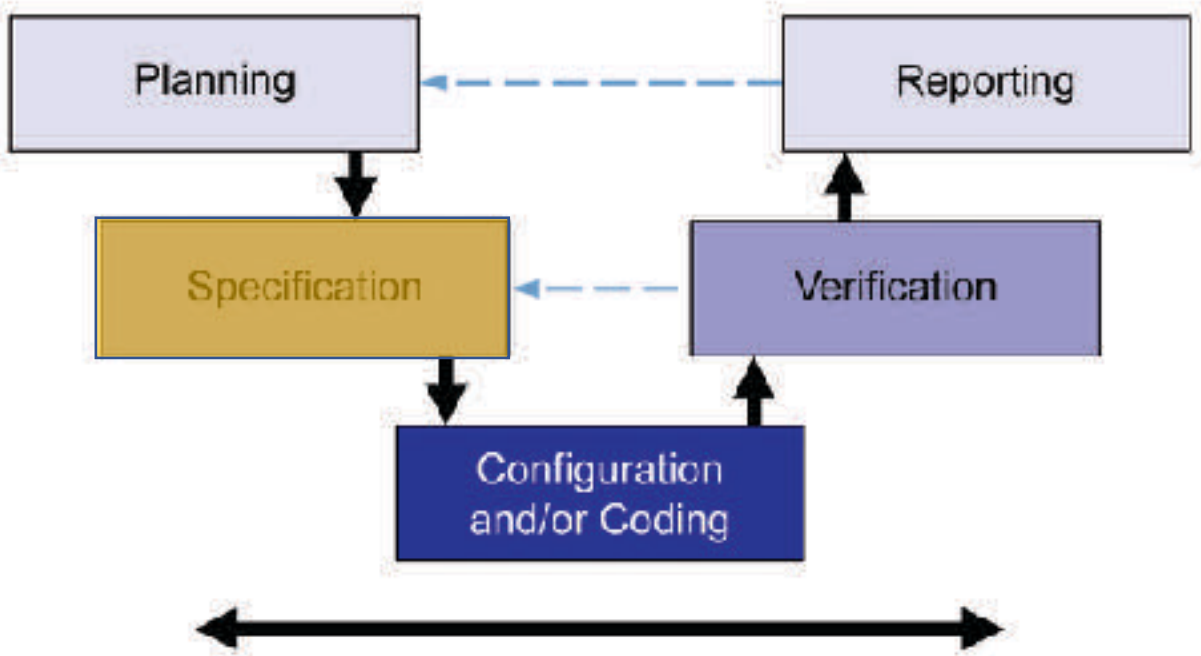
The Approach



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URS (User Requirement Specification) – The Client

In order to ensure a cleanroom monitoring system meets your requirements defined in the process risk assessment, developing a thorough URS is critical. A URS should cover elements such as;

- Critical process measures (i.e non-viable particulate, temperature etc.)
- Where monitoring is to take place within the facility by parameter.
- Performance expectations and tolerance thresholds.
- Warning and action limits.
- Data recording and logging expectations.
- Interface requirements (fixed HMI, web-based, application based etc.)
- External interfaces (BMS, FMS & Server integration)

Think S.M.A.R.T (Specific, Measurable, Achievable, Realistic, Testable)

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System Considerations – Where should I monitor

In order to gain the most representative room operational data set, considering where you should monitor is critical. Things to consider;

- Map the process flow to define critical monitoring locations
- Consider what are the critical process parameters by room/zone
- Determine external influences on monitoring data

System Considerations – Performance parameters and tolerances

It is critical to outline what is to be monitored and to what tolerance this parameter is to be measured for a number of reasons such as;

- Instrumentation sensitivity
- Data logging frequency
- Alert and action limit expectations
- Graphical User Interface (GUI) and dashboard layouts

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System Considerations – Data Recording and logging

Whether through a manual recording process or automated data gathering, understanding how you are going to interact with and store data is paramount. Depending on the industry and application there is a lot to consider;

- How secure is the data? (is there any CFR21 Part 11 requirements)
- How is it to be stored?
- Does the data require backing up?
- How long do I need to retain my data records for?

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System Considerations – Interfaces

At either an instrument or system level, it is important to understand how you will expect people to interact with the monitoring data being generated from the system or device.

- Is there local instrument displays?
- Does the system require a fixed HMI or display?
- Will the system be cloud based and be accessible remotely?
- How will people be made aware of ‘out of specification’ events?

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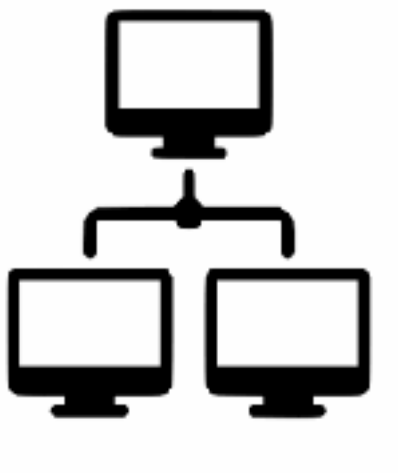
System Considerations – Links to external systems

With developments through Industry 4.0 and IoT it is important to consider any links required to external systems when specifying a system such as;

- Is there an overarching Building Management System?
- Is there a requirement for data to be pushed to a server?
- Should the system use Windows login credentials for access controls?



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What system do I need?

There are a broad range of instrumentation and systems available in the market to service all of your monitoring needs and the process considerations I have just described should help determine which path you should go down.

- Standalone instrumentation
- PLC control system
- PC based platform
- Web based application

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To summarise

- A thorough risk assessment of the process is key
- Understand the governing legislation
- Produce a clear, well defined URS
- Explore what is available in the market place.

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Thanks for listening