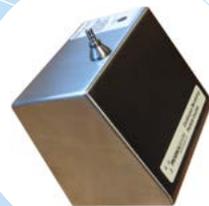


Pharmagraph

enVigil-IMS
Isolator
Monitoring
System



PHARMAGRAPH
Pharmaceutical Monitoring Systems

Pharmagraph have been providing particle monitoring systems since 1992 and have a wealth of experience in supplying application specific solutions for pharmaceutical aseptic production facilities manufacturing in an FDA/EU-GMP compliant environment.

From a sterility test isolator to a multiple zone integrated filling machine isolator Pharmagraph have a range of system solutions to meet the ever-demanding needs of the pharmaceutical industry. Isolator and filling machine manufacturers traditionally provide bespoke isolator filling machines for specific products and production facilities. However, things are changing, to meet the challenges of a diversified market, providing better flexibility and in an effort to drive down costs.

Filling machine and isolator manufacturers now also offer multiple format options allowing a single filling machine and isolator to provide multiple filling formats such as vials, syringes and ampoules all of which are provided in an H2O2 gassed decontamination environment.

The advent of this new isolator technology and the drive towards system flexibility presents new challenges for the particle monitoring system supplier. There is a need to ensure that the particle monitoring system offered addresses the adaptable requirements of the production facilities now being provided. With this new modular isolator filling machine, then production facilities are able to quickly adapt to different products and

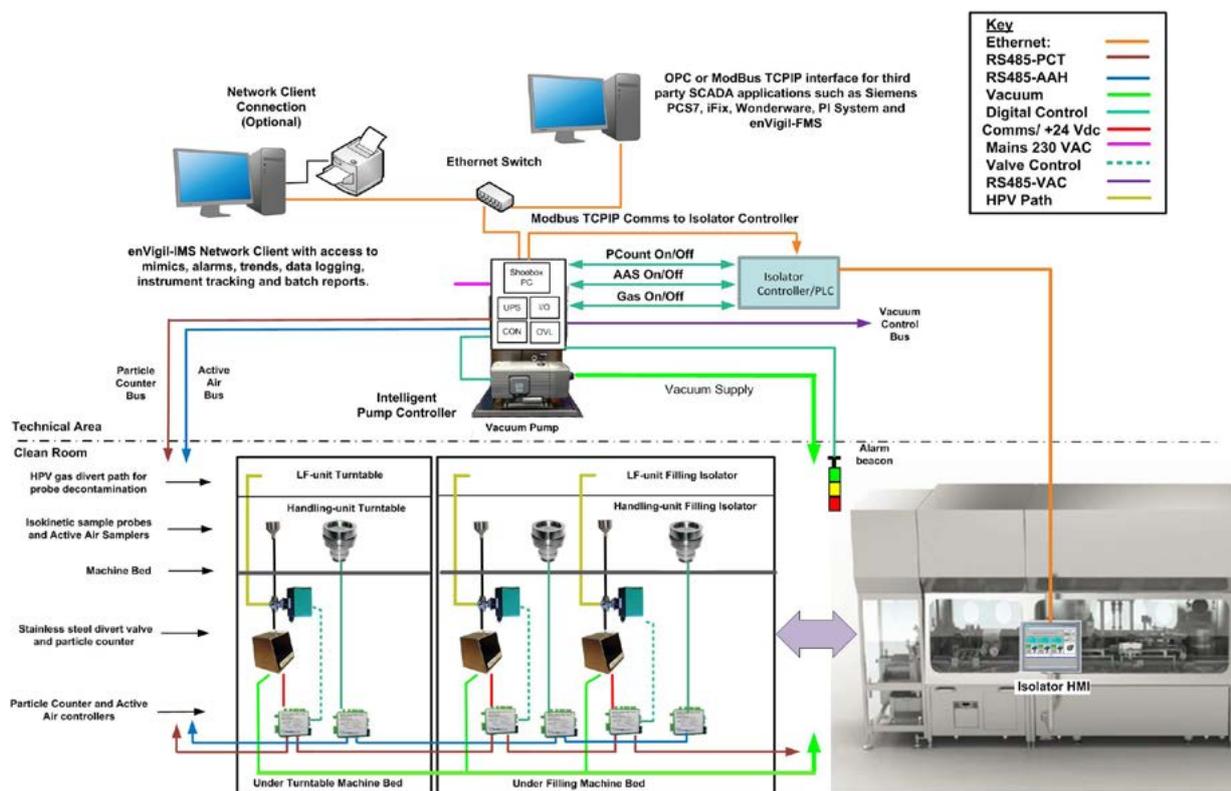
batch sizes in the shortest possible time. This provides better production flexibility which in turn leads to reduced plant investment and therefore a significant reduction in cost.

This production modularity requires the particle monitoring system supplier to adopt a more considered and holistic approach to their system offering. The particle monitoring system sampling points for non-viable and viable samples are determined through risk assessment to meet the requirements of FDA/EU-GMP requirements. This risk assessment may well be conducted by the pharmaceutical customer in association with the filling machine/isolator manufacturer and particle monitoring system supplier.

This is to determine the most suitable and practical sampling positions that will satisfy the regulatory inspectors and meet the FDA/EU-GMP requirements.

To meet these new challenges, Pharmagraph have developed a new range of system solutions that will address both the traditional bespoke isolators and the new modular integrated isolator filling machines.

ENVIGIL- IMS : ISOLATOR MONITORING SYSTEM

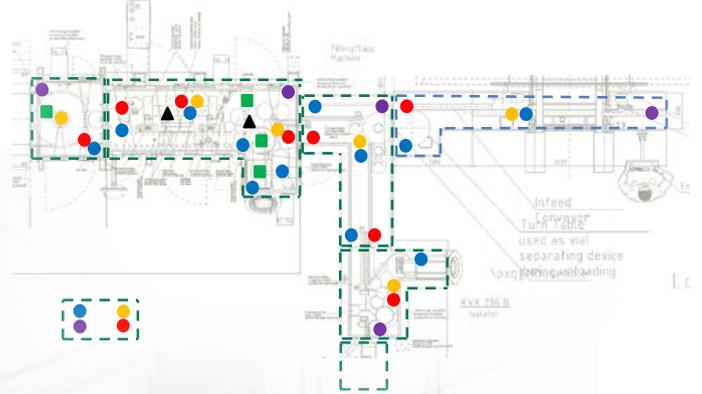


enVigil-IMS Isolator Monitoring System

enVigil-IMS (Isolator Monitoring System) offers an integrated platform that provides particle monitoring, active air sampling, hydrogen peroxide protection for the particle counters, alarm notification, instrument tracking and multiple connectivity interfaces.

Line Layout – Monitoring Locations

- Active Air Sampler
- Particle Counter
- Settle Plates (Monitoring)
- Settle Plates (Classification)
- Contact Plates (Critical Surfaces and Gloves)
- ▲ Swaps (Filling Needles, Stopper Guides and VHP Load Point Contacts)



Intelligent Pump Controller

Intelligent Pump Controller

The heart of the enVigil-IMS system is the intelligent pump controller and this is located in the technical area, normally above the cleanroom facility. The intelligent pump controller contains an integrated shoebox PC running the enVigil-IMS application software. The intelligent pump controller is able to monitor and control up to five continuous particle counters – supplied by a central vacuum pump, five active air samplers and a digital control interface to the isolator filling machine PLC. The enVigil-IMS application provides an operator screen on the isolator filling machine human machine interface (HMI). This enables the operators to easily monitor and control the system, including acknowledging alarms and managing their filling machine operations.

For isolator applications with more than five continuous sampling positions there is an extension module known as the Slave Pump Controller which provides up to two or four additional particle counter and active air sampling positions.

If the filling machine has multiple zones which require particle counters to be independently controlled, for example for freeze dryer and filling operations which may require independent operations. For these applications an optional vacuum control manifold can be supplied to support this requirement.

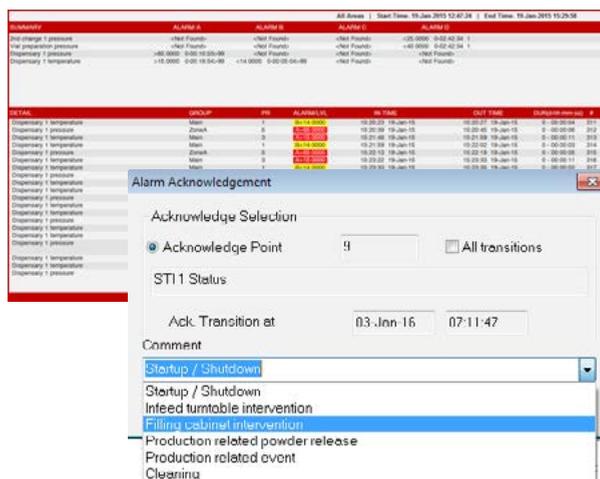
The enVigil-IMS application allows configuration of the system to include sampling point descriptors, alert (warning) and action (alarm) levels, counts per cubic feet and counts per

cubic metre for >0.5µm and >5.0µm size channels, hydrogen peroxide protection valves and instrument tracking facilities. The enVigil-IMS application provides a data historian function maintaining historic information for alarms, periodic data and audit logs, all of which are maintained in a 21 CFR Part 11/EU-GMP Annex 11 compliant environment.

Operators may acknowledge particle monitoring system alarms on the Isolator HMI. This provides a list of alarm reasons which are selected from a drop-down menu and also allows free text entry.

The intelligent pump controller has multiple communication interfaces allowing connectivity to the isolator HMI/PLC controller via a ModBus TCP/IP interface for operational functionality.

Host SCADA communications are also available via an OPC (Ole for Process Control) server allowing real



time data access to particle monitoring and active air sampling information to be passed to the on-site SCADA application. Typical SCADA applications would include iFix, Wonderware, Siemens PCS7, PI System, enVigil-FMS and many others.

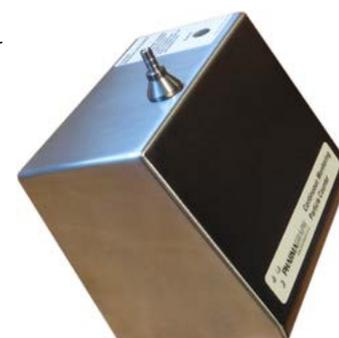
Non-Viable Particle Counters

The five continuous particle counter positions are supplied with a common vacuum source provided by a single vacuum pump. Typical sampling positions for an integrated isolator filling machine include accumulator turntable, filling head, vial transport conveyor, crimping station and other related Grade A zones. Each particle counter sampling position returns results as counts per cubic feet (28.3 L/min) and counts per cubic metre for >0.5µm and >5.0µm size channels.

Each particle counter is protected from hydrogen peroxide contamination by a stainless-steel diverter ball valve. When hydrogen peroxide vapour (HPV) gassing is required to decontaminate the isolator filling machine it is necessary to protect the particle counter from the HPV gas. Over time exposure to the HPV gas will “bleach” or leave deposits on the optics of the laser particle counter rendering it useless. Therefore, it is necessary to protect the particle counter inlet port to stop the ingress of HPV gas. This reduces system downtime due to particle counter sensor failure and protects system investment.

When HPV gassing is required the isolator signals the intelligent pump controller and the stainless-steel ball valve is switched to the “Divert” position by the particle

counter controller. The particle counter controller monitors the transition of the valve and when it reaches the “Divert” position then a “Clear to Gas” signal is sent to the isolator controller. This then initiates the HPV gassing decontamination of the filling line.



The continuous particle counter also offers “Swap-Ability” which means that each particle counter can be swapped in and out of service without the need for re-programming the location address. This offers a quick and efficient method of replacing the particle counter when maintenance or calibration service is required.

The deployment of each particle counter is also tracked by the unique serial number of each device by the instrument tracking software which is included with the enVigil-IMS application.

Viable Active Air Sampling

The enVigil-IMS system offers active air samplers which are mounted in predefined sampling positions as determined by the risk assessment. The Pharmagraph air sampler provides an integral fan impeller which is monitored and controlled to maintain the correct sample volume and D50 value. The Pharmagraph active air sampler is provided in 316 grade stainless steel and is provided with an easy fit sieve head with either a pedestal base or a tri-clamp mount.

The Pharmagraph active air sampler is monitored and controlled to a calibrated 100 L/min flow rate and achieves a D50 value of less than 2.0µm. Active air sampling can be provided as either a continuous sample to acquire a 1000L sample in one duration or can be programmed to be an interrupted sample over a longer time period. The major

benefit of using the Pharmagraph active air sampler for isolator based applications is that the sampled air remains within the isolator and there is no need for an external vacuum system with all the vacuum system infrastructure and cost that entails.

The deployment of each Pharmagraph active air sampler is also tracked by the unique serial number of each device by the instrument tracking software which is included with the enVigil-IMS application.



Instrument Tracking

The enVigil-IMS system offers a unique instrument tracking facility. Provision of this instrument tracking facility enables both production and QC personnel to know which instruments were used in which sampling positions. Therefore, if there are any production related issues, which involve the particle monitoring system, then the

instrument tracking facility can assist in the identification and root-cause investigation of any instrument failings. The instrument tracking facility also offers "Calibration Due" alerts (warnings) and actions (alarms) which will alert production personnel of an instrument calibration service becoming due.

Instrument Report

Report for: Counters Start Date/Time: 12 September 2011 16:50:22 End Date/Time: 19 September 2011 16:50:22

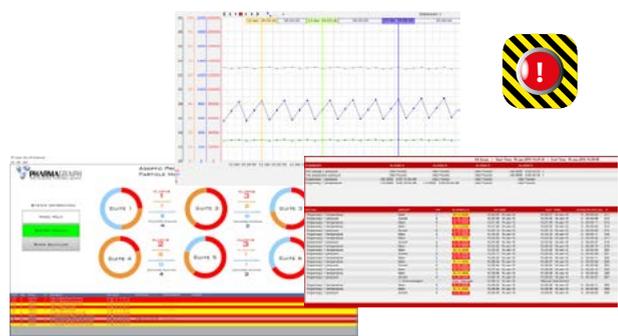
Position	Deployment Start	Deployment End	Manufacturer	Model	Serial Number	Inst. Type	Calibration Status
Infeed	16-Sep-11 16:05	16-Sep-11 16:07	Hach	6015	1108158009	Particle Counter	In Cal
	16-Sep-11 16:07	16-Sep-11 16:08	Hach	6015	1108158007	Particle Counter	In Cal
	16-Sep-11 16:10	16-Sep-11 16:11	Hach	6015	1108158009	Particle Counter	In Cal
	16-Sep-11 16:11	16-Sep-11 16:14	Hach	6015	1108158007	Particle Counter	In Cal
	16-Sep-11 16:14	-----	Hach	6015	1108158009	Particle Counter	In Cal
Filling	16-Sep-11 16:08	16-Sep-11 16:11	Hach	6015	1108158007	Particle Counter	In Cal

System Expansion

Network client connections can also be provided allowing access to the real time and data historian server which are available within the enVigil-IMS application. These provide facility mimics, real time and historic trends and batch reports with full network clients offering site-wide access.

The enVigil-IMS application also offers optional modules for ODBC/SQL database table exchange. This enables the transfer of SQL data from the enVigil-IMS data, alarm and audit log files to a third-party ODBC/SQL database. The enVigil-IMS application includes the batch reporting package which can be optionally enhanced to support electronic signatures. The batch reports then incorporate electronic sign off for operators, supervisor review and QC approver status for the batch completion and release of the manufactured product.

enVigil-IMS can also be integrated into a wider enVigil-FMS based Facility Monitoring System. Multiple isolator filling lines running the enVigil-IMS application can be connected together and into an enVigil-FMS Host Server to provide a site-wide view of the whole production facility.



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