Clarity in GMP Guidance notes

PHSS Clarity of GMP Guidance notes.

1. **Assurance of sterility in Aseptic manufacturing of surfaces that contact product contact parts** e.g. Stopper contact surfaces. Relates to MHRA Blog on fragility of VHP.

2. **Localised uni-directional airflow: L-UDAF** as protection from airborne contamination transfer within a classified zone. L-UDAF is applied where airflow protection is required outside applications of capping filled vials where specifically Grade A air flow applies to Capper zones (Annex 1 requirement).

   L-UDAF applies to Isolator 'Mouse holes', Autoclave load/unload, Lyophilized – Freeze dryer load/unload etc. where contamination risks are much higher than in capping where product containers are already closed.

3. **Barrier Leak rates and leak Integrity** applied to Barrier systems relative to contamination risks in Aseptic processing and containment of hazards.

   ISO standards in this area of barrier systems leak integrity are out of date as new barrier technology has developed at major filling line scales where both aseptic conditions in contamination control and containment are required for highly toxic products including Antibody drug conjugates (ADCs) that require Aseptic-containment at new OEB6 levels.

4. **Continuous particle monitoring** in controlled areas including GMP compliance monitoring (at 1m3 sample volume) monitored in a 36 minute 'walking window' and contamination event monitoring (at 1ft3 sample volume) with sequenced 1 minute sample trending that consider deviations at warning, alert and action levels to report a contamination event.

5. **Airflow visualisation** of uni-directional airflow in GMP controlled zones including barrier systems considering CFD: computational fluid dynamics, Smoke visualization studies and LR Method (smoke particle challenge with tracking of particle movement via particle counting).

6. **Avoiding Wet loads in Moist heat sterilisation**.

7. **Glove management strategy for Barrier system gloves-sleeves** as a Life cycle including selection, integrity testing (visual and physical) and response to post batch glove leak detection.

8. **VHP/vH202 surface Bio-decontamination of loads** in Barrier Isolator technology and Material transfer chambers including qualification studies with biological indicators (BIs) and requirements for correlation studies for enzyme indicators (EIs).

9. **Definitions of 'Open and Closed' applied to Aseptic processing**, Isolator barrier systems, RABS; Restricted Access Barrier Systems and sterile product processing.