Annex 1 and Uni-directional Airflow Systems
Working Height Velocity (WHV)

Gordon Farquharson
June 2012
• Agenda- Uni-directional Airflow Systems

• Regulatory requirements & expectations.
• Measurement methods.
• Location and level of measurement.
• Case study of working height evaluation.
• Monitoring vs Certification
• Discussion forum
  – Velocity limits & ranges.
  – The role of airflow visualisation.
  – Airflow uniformity.
  – Test & monitoring locations & frequency.
Some common problems with UDAF systems

- Poor airflow uniformity leads to turbulent airflow and vortex formation.
- 50 & 75 mm (2-3 in) deep mini-pleat filters don’t control airflow as well as old 150 mm (6 in) deep pleat filters did. Plenum and fan design is much more critical.
- Under-sized filters fail the in-situ aerosol leak test.
- Inappropriate airflow visualisation.
- Lack of agreement about the measurement plane/level.
- Experience that velocity seems to reduce if you measure at different heights down from the filter.
Airflow Control Devices

- Plenum
- HEPA
- Mounting frame
- Tear-drop Light
- Laminator Membrane

[Diagram of airflow control devices with annotated parts]
UDAF Guidance - EU

- **Grade A**: The local zone for high risk operations, e.g. filling zone, stopper bowls, open ampoules and vials, making aseptic connections.

- Normally such conditions are provided by a laminar air flow work station. Laminar air flow systems should provide a homogeneous air speed in a range of 0.36 – 0.54 m/s (guidance value) at the working position in open clean room applications.

- The maintenance of laminarity should be demonstrated and validated.

- A uni-directional air flow and lower velocities may be used in closed isolators and glove boxes.

**This same as 0.45 +/- 20%**

**Important working position. How to interpret this ???**

**Means airflow visualisation**

**Recognises performance ahead of velocity**
• HEPA-filtered air should be supplied in critical areas at a velocity sufficient to sweep particles away from the filling/closing area and maintain unidirectional airflow during operations. The velocity parameters established for each processing line should be justified and appropriate to maintain unidirectional airflow and air quality under dynamic conditions within the critical area (Ref. 3).

Proper design and control prevents turbulence and stagnant air in the critical area. Once relevant parameters are established, it is crucial that airflow patterns be evaluated for turbulence or eddy currents that can act as a channel or reservoir for air contaminants (e.g., from an adjoining lower classified area). In situ air pattern analysis should be conducted at the critical area to demonstrate unidirectional airflow and sweeping action over and away from the product under dynamic conditions. The studies should be well documented with written conclusions, and include evaluation of the impact of aseptic manipulations (e.g., interventions) and equipment design. Videotape or other recording mechanisms have been found to be useful aides in assessing airflow initially as well as facilitating evaluation of subsequent equipment configuration changes. It is important to note that even successfully qualified systems can be compromised by poor operational, maintenance, or personnel practices.

• A velocity of 0.45 meters/second (90 feet per minute) has generally been established, with a range of plus or minus 20 percent around the setpoint. Higher velocities may be appropriate in operations generating high levels of particulates.
UDAF Guidance - FDA.

UDAF Velocity

- States performance expectation.
- *Air in critical areas should be supplied at the point of use as HEPA-filtered uni-directional air-flow at a velocity sufficient to sweep particles away from the filling/closing area and maintain unidirectional airflow during operations. The velocity parameters established for each processing line should be justified and appropriate to maintain unidirectional airflow and air quality under dynamic conditions within a defined space.*
Managing the differences UDAF Velocity EU vs FDA.

- The basic requirements are fundamentally the same.
- Regulators are comfortable with 0.45 m/s (90 fpm) +/-20%; other velocities are OK; if you plan to use something different, ensure the rationale and justification is sound.
- Recorded “operational” airflow visualisation is the norm.
- Be clear about the height at which the velocity is to be measured.
- GEP – Good Engineering Practice
  - Should includes consideration of system & filter velocity
  - Use airflow visualisation to help assess the test and working level measurement points.
Monitoring & Testing Methods & Frequency
Velocity Measurement Methods

• Anemometers
  – Vane
  – Hot wire

• Location
  – Perpendicular to the airflow source plane
  – Min 50 mm (2 in) from filter face
  – Other defined test plane

• Frequency
  – Qualification ~ typically 6 monthly (integrated with filter testing)
  – Monitoring ~ weekly for low tech methods ~ continuous fixed monitoring systems
Airflow Visualisation Methods

• Video record.
• Isothermal aerosol (smoke). Water vapour or propylene glycol.
• Should include operations and interventions.
• Choreograph the visualisation.
• May need aids to improve optical contrast.
• Pulsed aerosol source can help visualise velocity.
• Multiple nozzles helps visualise parallelism of flow.
• **Frequency** – At system qualification and after significant system or process change.
System & Filter face velocity

Can be very different, and the difference is important
Uni-directional Airflow Velocity

UDAF - Filter Grid

Filter vel 25-50 mm from filter face

System vel 100-150 mm from filter face

Work Height vel 100-150 mm from filter face
Eli Lilly in Indianapolis have undertaken some studies to examine the challenge of determining and measuring velocity in UDF at “working level”.

In these slides, **WHV = “working height velocity”**

The next slides are a summary of this work. Eli Lilly (Tom Spearman & Don Moore) have made this information available.
Anemometers

- Previous studies used a Shortridge Velgrid Anemometer with minimum velocity of 50 fpm
- Vane anemometers are also relatively insensitive.
- These Eli Lilly studies used a TSI Thermal Anemometer with minimum velocity of 3 fpm (much more sensitive)

Instrument image from TSI
• Ten second time constant is acceptable
• No relevant variability in readings due to flow rate
• Anemometer must be fixed held and near-perfectly aligned for rotation
• Visual alignment for probe tilt is acceptable
• Operator to operator variability is negligible
Thermal Anemometer Probe Orientation

Rotation

Tilt
Accumulator Table WHV Data Collection

Normal Flow at Working Height
(Eli Lilly – Indianapolis Study)

Heading = "Area A Normal Flow"

Average

Standard Deviation

Coefficient of Variability

Represents 6” x 6” grid, with critical location in center.

Coefficient of Variability = Standard Deviation/Average
Normal Flow Air Column Results

- **4” Below Filter Face**
- **16” Below Filter Face**
- **28” Below Filter Face**
- **Working Height**
General Conclusions

- The type and sensitivity of type of measurement instrument has a huge effect on velocity measurement.
- Individual WHV readings are very dependent upon the internal geometric shape of the items in the critical area
  - Thermal anemometer measurements can be reproduced when following a consistent method
- Small changes in the X – Y – Z planes cause significant variation in the individual reading
  - Variability in readings are shown to be a result of the process and not the anemometer
- Individual readings do not provide for a sufficient indication of the overall system performance
- It is important to determine a good test level and prove effectiveness of the clean air system by airflow visualization.
• Requirements
  – WHV locations must be identified by Sterility Assurance.
  – WHV acceptance limits must be established for Grade A UDF hoods for each location
  – WHV must to be conducted under the same conditions as airflow pattern testing.
  – WHV limits must be established by measuring hood velocities at minimum, maximum, and set point.
  – Once WHV acceptance criteria have been established for a hood, routine verification must occur on a periodic basis.
Thanks for your attention Questions???
PharmOut
Unit 20, 40 Montclair Avenue,
Glen Waverley,
Victoria,
Australia, 3150
Tel +61 (0) 3 8610 0169

Thanks for your attention
Gordon J Farquharson
Chair BSI LBI/030; Chair CEN TC243; Convenor ISO TC209 WG1.
c/o Critical Systems Ltd
www.critical-systems.co.uk
4, Greencroft, Guildford, Surrey, GU1 2SY, UK.
tel +44 (0)1483 579926
mob +44 (0)7785 265 909
e-mail gj.farquharson@gmail.com & gjf@critical-systems.co.uk
This presentation has been prepared and delivered by:-

Gordon J Farquharson
Critical Systems Ltd
Consulting in Safety & Quality Critical Systems

Guildford, Surrey, GU1 2SY, UK

cell +44 (0)7785 265 909
e-mail gj.farquharson@gmail.com