# Comparison of Deposition Efficiency and Uniformity of Monodisperse Solid Particle Deposition in Two Air Liquid Interface (VITROCELL® 24/48 and AMES 48) In-Vitro Exposure Systems with Computational Fluid Dynamic (CFD) Predictions

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## Abstract

For toxicological assessment of inhalable chemicals, in-vitro exposure systems that enable aerosols to be delivered directly to the apical surface of respiratory cells (air liquid interface; ALI) provide a more realistic exposure method than traditional submerged in-vitro cultures. Quantitative aerosol dosimetry (delivered dose) is critical for interpretation of biological results generated from these ALI in-vitro exposure systems, comparison with existing literature, and potential extrapolation to human exposures. Using two commercially available ALI in-vitro exposure systems (VITROCELL® 24/48 and AMES 48), particle deposition efficiency and uniformity of deposition across the cell culture inserts and petri dishes were experimentally quantified and compared with CFD predictions. Four diameters of monodisperse fluorescent particles (0.51, 1.1, 2.2, and 3.3 μm mass median aerodynamic diameter) were used in the experimental measurements (2 h). Lagrangian and Eulerian CFD techniques using the experimental airflow rates and the identical geometry were performed for the VITROCELL® 24/48. For the VITROCELL® 24/48 exposure system (Figure 1), experimentally measured particle deposition efficiency via fluorescent microscopy ranged from a mean (N = 3 runs) of 0.013% to 0.86% as a function of particle diameter (Table 1). Variability in the uniformity of particle deposition across the cell culture inserts was observed and ranged from 40% to 150% of the mean number of particles/mm² within a single experimental run. Mean deposition variability across the cell culture inserts (Figure 2) in a row for each particle size are shown in Figure 3. There was good agreement between experimentally measured and Lagrangian and Eulerian CFD predicted particle deposition efficiency and Lagrangian CFD predicted uniformity of particle deposition for the VITROCELL® 24/48 exposure system (Table 1 & Figures 3 & 4). For the VITROCELL® AMES 48 exposure system, three different sampling flowrates (5, 10, and 20 cc/min) were evaluated experimentally, with the 10 cc/min sampling flowrate providing the most consistent number (65%–135% of mean number of depositing particles) of deposited particles, regardless of particle size (Figure 5). Experimentally measured deposition efficiency (10 cc/min flowrate) ranged from a mean (N = 3 runs) of 0.07% to 0.43% as a function of particle diameter (Table 2). Variability in the uniformity of particle deposition (Figure 4) across the petri dishes was observed (Figure 6). Preliminary CFD predictions (Lagrangian and Eulerian) agree with the experimental results.


**FIGURE 1.** Vitrocell® 24/48 top plate (A) showing aerosol inlets/outlets on the sides, horns through which the aerosol flows and the perimeter exhaust and bottom plate (B) showing where the cell culture inserts are placed (pictures are courtesy of Vitrocell® GmbH).

**TABLE 1.** Comparison of Experimentally Measured (N=3) and CFD Predicted Deposition Efficiency

| Particle MMAD (μm) | Particle Deposition Efficiency % - Vitrocell® 24/48 | | | | |
|---|---|---|---|---|---|
| | Experimentally Measured | | CFD Predicted | | |
| | Mean | SD | Lagrangian | | Eulerian |
| | | | Mean | SD | |
| 0.51 | 0.013 | 0.009 | 0.012 | 0.005 | 0.015 |
| 1.1 | 0.06 | 0.03 | 0.045 | 0.007 | 0.064 |
| 2.2 | 0.29 | 0.08 | 0.153 | 0.01 | 0.221 |
| 3.3 | 0.86 | 0.24 | 0.376 | 0.026 | 0.496 |

SD = standard deviation

## Results

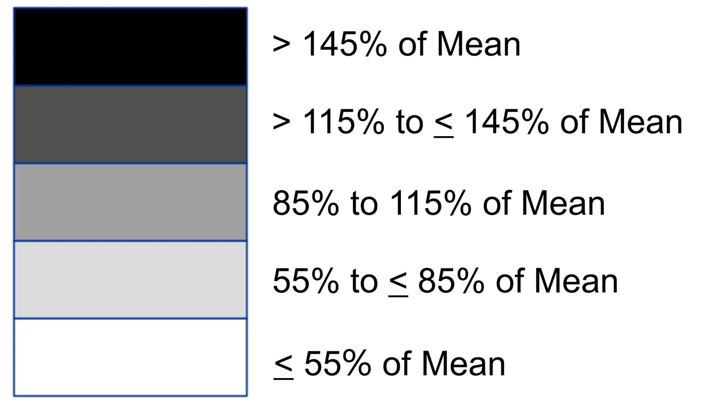


**FIGURE 2.** Shading scheme as percent of mean for deposition uniformity in the four equal area quadrants and circle and 3 rings of equal area for both ALI in-vitro exposure systems as shown in Figures 3, 4, & 6.

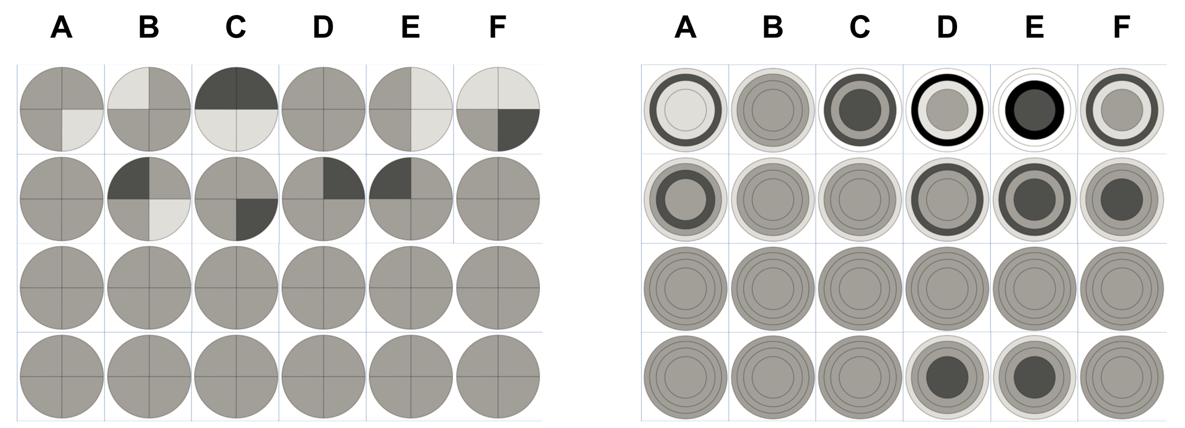


**FIGURE 3.** Experimentally measured (mean of three experimental runs) particle deposition uniformity across cell culture inserts in Vitrocell® 24/48 ALI in-vitro exposure system by particle size (top = 0.51, second = 1.1, third = 2.2, and bottom = 3.3 μm) in four equal area quadrants (left) and circle and 3 rings with equal area (right).

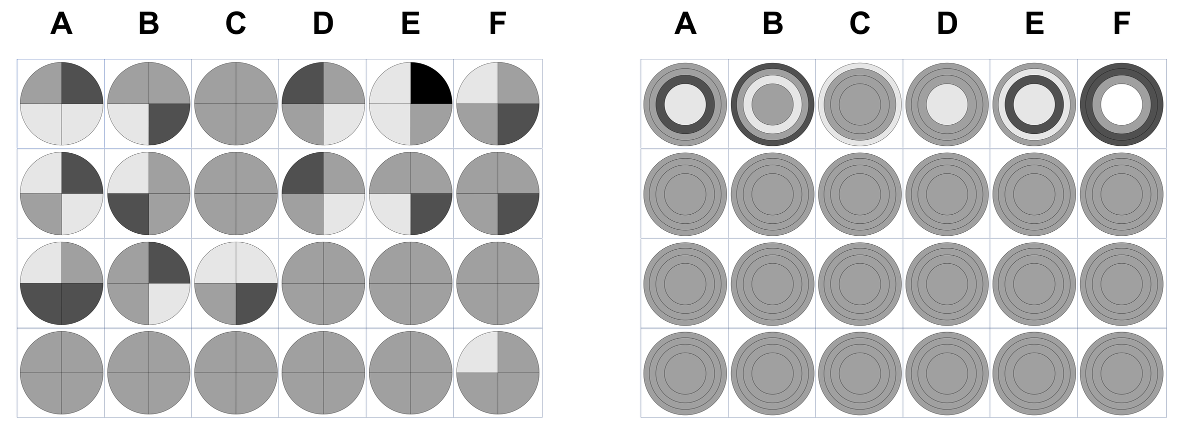


**FIGURE 4.** Lagrangian CFD predicted particle deposition uniformity in a row of cell culture inserts in four equal area quadrants (top = 0.51, second = 1.1, third = 2.2, and bottom = 3.3 μm) and in a circle and 3 rings with equal area.(top = 0.51, second = 1.1, third = 2.2, and bottom = 3.3 μm). One million particles were injected at the entrance of the Vitrocell® 24/48 ALI in-vitro exposure system.

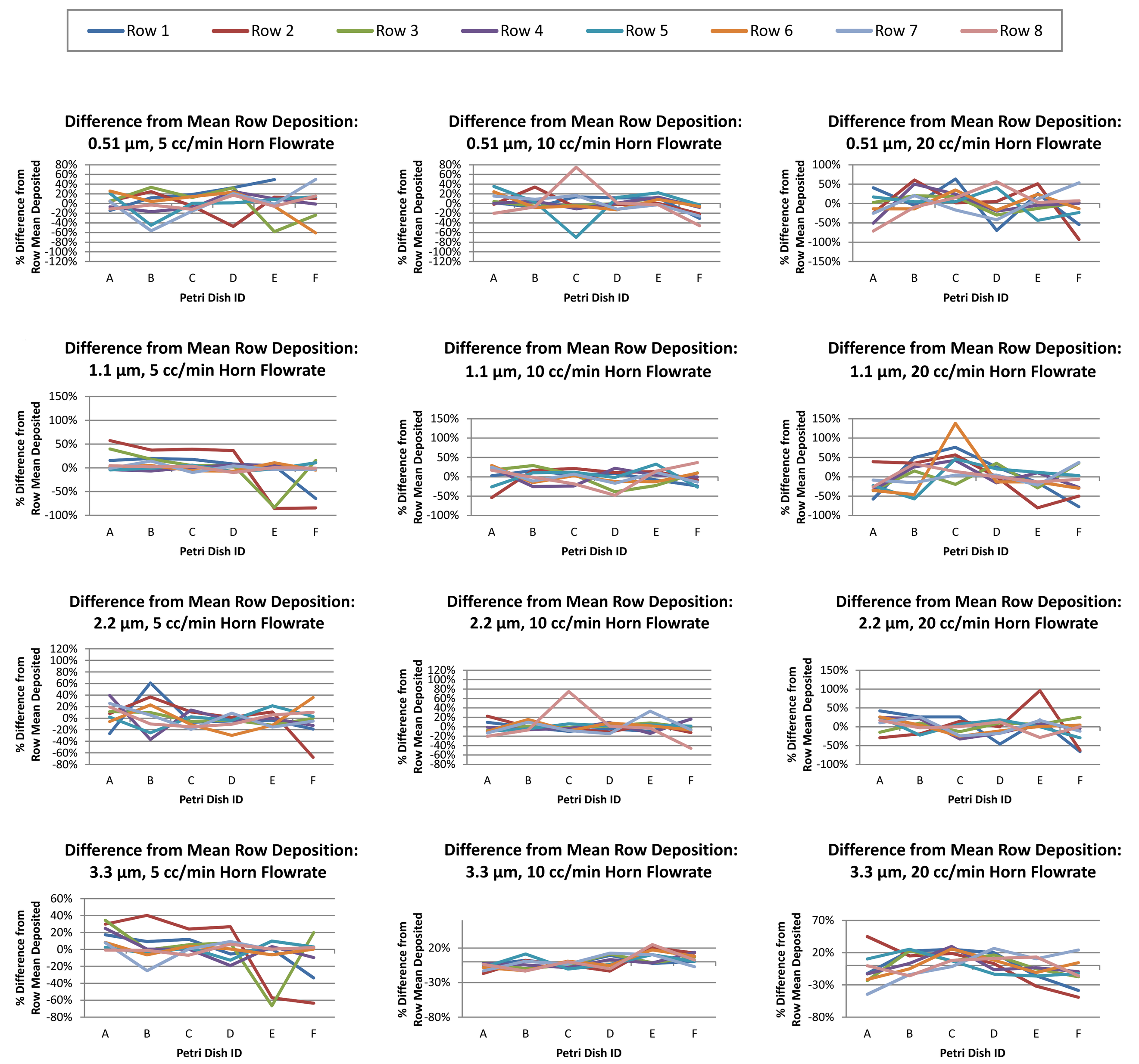


**FIGURE 5.** Vitrocell® AMES 48 variability in particle deposition as a function of horn flow rates of 5, 10, or 20 cc/min.

**TABLE 2.** Experimentally Measured (N=3) Deposition Efficiency (Mean ± Standard Deviation)

| Particle MMAD (μM) | Particle Deposition Efficiency % Vitrocell® AMES 48 | |
|---|---|---|
| | Experimentally Measured | |
| | Mean | SD |
| 0.51 | 0.07 | 0.03 |
| 1.1 | 0.08 | 0.02 |
| 2.2 | 0.24 | 0.17 |
| 3.3 | 0.43 | 0.13 |

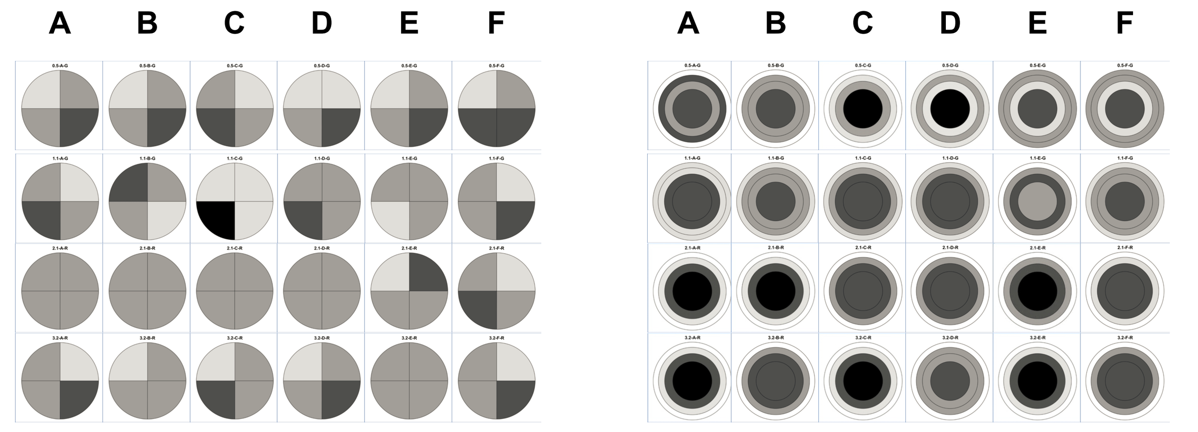


**FIGURE 6.** Vitrocell® AMES 48, horn flowrate = 10 cc - experimentally measured particle deposition uniformity across petri dishes by particle size (top = 0.51, second = 1.1, third = 2.2, and bottom = 3.3 μm) in four equal area quadrants (left) and circle and 3 rings with equal area (right).

## Implications

Our deposition efficiency and uniformity of particle deposition results apply only to solid particles. Also, Lagrangian CFD predictions of uniformity of particle deposition varied as a function of number of injected particle up to 100,000 particles. Therefore, the results should not be used to directly extrapolate the deposition characteristics of liquid droplet aerosols such as e-vapor that will likely spread after depositing. Caution is needed in extrapolating the particle results to e-vapor aerosol that contains both liquid droplets and vapors.

The particle deposition efficiencies determined for each ALI exposure system can be used to calculate a range of realistic potential particulate target doses or calculate the amount of starting material required to achieve a specific particulate target dose. Quantitative aerosol dosimetry in these two ALI exposure systems enables quantitative exposure characterization and a basis for future dosimetry extrapolation to human exposures.

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