ABSTRACT
Modern drug discovery and research labs are utilizing complex automation systems to assist in high throughput screening of novel drug candidates. One of the primary sources of error in this process can be attributed to faulty liquid handling of automated liquid handlers. This, in turn can wreak havoc on data management systems and downstream processes which may result in costly false positives or negatives. As an early warning system to reduce the risk of erroneous pipetting and to ensure sample volume quality, a pressure based volume measuring system for micro-plates has been developed. The Artel VMS™ is able to accurately and precisely detect 0 - 500 µL volumes in 96 or 384 well plates without directly contacting the liquid. The unique pressure based volume detection method allows the instrument to be unaffected by sample color, well shape, plate type, or sample material. This enables the device to overcome the weaknesses experienced by current volume detection methods (gravimetric, capacitance, optical, or infrared).

HOW THE VMS WORKS
The Artel VMS extends its stage to a plate loading position. A robotic XY stage moves the microplate column-wise under the sensor manifold. The Z-axis stage lowers the manifold over the well creating a seal.

A measurement channel consists of a stainless steel syringe connected to a manifold, a digital pressure sensor, and a compliant seal that mates with the well. 8 wells are read at once.

A calibration curve is generated by reading the pressure in multiple empty and full wells on the desired plate type. A line is created between the empty well pressure and the full well pressure. Volume readings are extrapolated from this line.

EXPERIMENT
MATERIALS AND METHODS
Tissue Culture Grade Water (Sigma W3500)
DMSO (EMD MX1457-7)
Greiner 384 well plate (781280)
Rainin P100 multichannel pipettor
Artel VMS

Water and DMSO was pipetted using a calibrated manual pipettor into a Greiner 384 well plate. 50 µL of water was dispensed into columns 1-12 and 50 µL of DMSO into columns 13-24. The plate was read 3X using the VMS (Initial read). The plate was then read 3X every hour for a total of 7 hours. Between time points, the plate was left on the deck of the VMS in the laboratory. (Average temp = 23.5°C, Average humidity = 23%, Average Pressure = 740mm Hg)

Can the VMS detect minute changes in solvent volume due to evaporative and absorptive properties of liquids in a 384 well plate?

EXPERIMENTAL SUMMARY
The VMS was able to detect small changes in volume over the course of a 7 hour test. The water side lost an average of 21% (10.5 µL) while the DMSO side gained an average of 4% (2 µL).

There was an obvious “edge-effect” on the water side of the plate where percentage loss reached a maximum of 28% (14 µL). It was also observed that the DMSO column along the water/DMSO interface (column 12 and 13) increased an average of 7% (3.5µL).

The heat map shows the final % loss or gain during the 7 hour test.

RESULTS
The VMS demonstrates that pressure based measurements can be effectively used to determine volume levels in microplates with high precision and accuracy.

The VMS is easy to use and calibrate, and is currently being used by a variety of biopharmaceutical, pharmaceutical, biotech and research facilities. To date, over 30 plate types have been validated for use in:
- Mother/daughter plate QC
- Liquid class optimization
- Process optimization
- Pipette verification (handheld and automated)