APPLIED PHYSICS

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MANUFACTURER TECHNICAL STATEMENT

# CRF6 Suitability for Pharmaceutical Airflow Visualization

Scientific basis for passive / functionally neutrally buoyant tracer behavior of micron-scale ultrasonic water fog

Document No. AP-TS-CRF6-001 | Revision 1.0 | August 2026

## Manufacturer Position

Applied Physics has reviewed the relevant peer-reviewed airflow-visualization and particle-image-velocimetry literature, first-principles aerosol dynamics, current FDA aseptic-processing guidance, and recent FDA warning-letter language concerning the use of neutrally buoyant media in airflow visualization studies.

Based on that evidence, Applied Physics concludes that micron-scale water fog generated by ultrasonic atomization is scientifically capable of functioning as a passive, functionally neutrally buoyant airflow tracer when the complete release configuration is qualified to demonstrate that gravitational settling, particle inertia, thermal plume effects, and source momentum do not materially bias the airflow being visualized.

**Key regulatory point:** Ultrasonic atomization is a generation mechanism. It is not, by itself, a scientific criterion for determining whether the resulting tracer adequately follows airflow. The relevant performance question is the behavior of the generated tracer and the complete release system during the intended airflow-visualization study.

## CRF6 Design Basis

- Nominal ultrasonic operating frequency: approximately 1.65 MHz.
- Nominal fresh-generated water-droplet range: approximately 4–8 micrometers.
- The CRF6 is intended to generate visible micron-scale water fog for airflow visualization without combustion products or oil-based smoke residue.
- These are manufacturer design-basis values. Finished-device measurement and site/configuration qualification provide the strongest device-specific evidence.

## Independent Scientific Support

| Evidence | Finding | Relevance |
|---|---|---|
| Kennedy, 1987 | Ultrasonic-nebulizer water fog was suitable for airflow | Direct published support for ultrasonic water fog as an |

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| | visualization and demonstrated the airflow features visualized by mineral-oil smoke. | airflow-visualization medium. |
| Lozano et al., 2014 | A 1.65 MHz ultrasonic seeder generated 4–5 μm Sauter-mean-diameter water droplets and was successfully used for stereoscopic PIV of a gaseous flow. | Closely matches the CRF6 nominal frequency/droplet regime and demonstrates quantitative tracer use. |
| Ayati et al., 2014 | Approximately 6 μm water droplets were used as gas-phase PIV tracers; Stokes analysis supported treatment as passive tracers and measurements agreed with independent flow data. | Direct support for airflow fidelity of water droplets within the CRF6 nominal size regime. |
| Tsai et al., 2017 | Measured MHz ultrasonic atomization showed decreasing micrometer droplet diameter with increasing frequency, consistent with established capillary-wave theory. | Independent support for MHz ultrasonic generation of micron-scale droplets. |

## Qualification Boundary

Applied Physics does not represent that every ultrasonic fog plume is automatically suitable without qualification. Published work demonstrates that evaporative cooling can create plume-scale negative buoyancy even when individual droplets are sufficiently small to behave as passive tracers. Therefore, the finished CRF6 configuration should be qualified for the intended use, including droplet-size distribution, thermal behavior, source momentum, still-air drift, and representative dynamic smoke-study execution.

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## Recommended Regulatory Use

This statement may be included by a pharmaceutical or biotechnology facility as manufacturer technical support within an airflow-visualization qualification, CAPA, inspection response, or scientific justification. It should be accompanied by the facility-specific executed smoke study and, where applicable, the CRF6 finished-device qualification evidence.

### Controlled conclusion

**Applied Physics considers a properly operated and qualified CRF6 scientifically suitable for pharmaceutical airflow visualization when the tested configuration demonstrates tracer behavior that faithfully represents the local airflow over the observation interval. Within that qualified envelope, the micron-scale ultrasonic water fog may be described as a passive or functionally neutrally buoyant airflow tracer.**

This technical statement does not represent FDA approval, certification, or endorsement and does not replace the facility's responsibility to demonstrate adequate dynamic airflow visualization under actual operating conditions.

## Primary References

1. U.S. FDA. Sterile Drug Products Produced by Aseptic Processing—Current Good Manufacturing Practice. Guidance for Industry. 2004.
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4. Kennedy DA. Water fog as a medium for visualization of airflows. Ann Occup Hyg. 1987;31(2):255–259. doi:10.1093/annhyg/31.2.255.
5. Lozano A, González-Espinosa A, García JA, Calvo E, Barroso J, Barreras F. High flow-rate ultrasonic seeder. Flow Meas Instrum. 2014;38:62–66. doi:10.1016/j.flowmeasinst.2014.04.002.
6. Ayati AA, Kolaas J, Jensen A, Johnson GW. A PIV investigation of stratified gas–liquid flow in a horizontal pipe. Int J Multiphase Flow. 2014;61:129–143. doi:10.1016/j.ijmultiphaseflow.2014.01.008.
7. Tsai CS, Mao RW, Tsai SC, et al. Faraday Waves-Based Integrated Ultrasonic Micro-Droplet Generator and Applications. Micromachines. 2017;8(2):56. doi:10.3390/mi8020056.

## Authorization

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|---|---|
| **Authorized Applied Physics Representative** | _____ |
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| **Signature / Date** | _____ |