OnQ™

Aerosol Generator

Aerogen®


E030

How Does It Work?

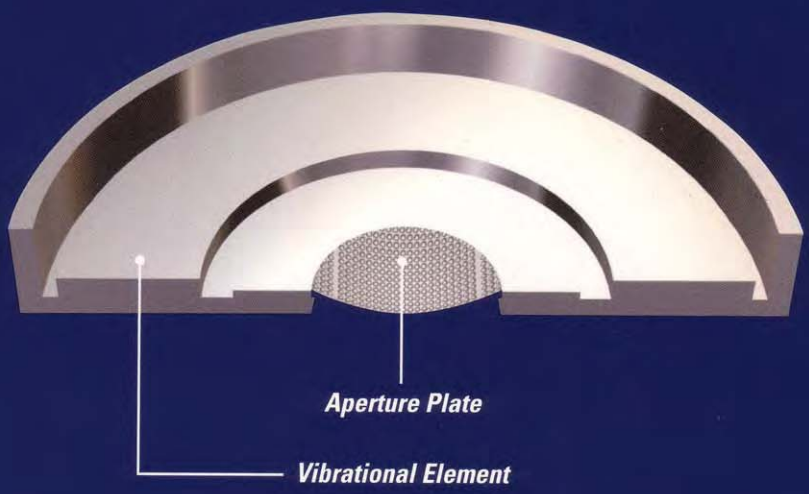
OnQ is an electronic micropump – a technology that produces liquid aerosol in a manner unlike any other technology currently available. As small as 3/8 inch in diameter and wafer-thin, OnQ is comprised of a unique dome-shaped aperture plate containing over 1,000 precision-formed tapered holes, surrounded by a vibrational element. When energy is applied, the aperture plate vibrates over 100,000 times per second. This rapid vibration causes each aperture to act as a micropump, drawing liquid through the holes to form consistently sized droplets. The result is a low-velocity aerosol optimized for maximum lung deposition.

OnQ aerosolizes efficiently, leaving virtually no residual liquid, and operates without using propellants or generating heat, thereby preserving a drug's molecular integrity. OnQ works with most pre-existing liquid formulations and can be customized for an individual therapeutic application by adjusting the particle size: a 3-4 micron particle size targets the lungs for respiratory therapy, and a 1-2 micron particle size targets the deep lung for systemic delivery. Combined, these advantages make OnQ ideal for delivery of a broad range of drugs including small molecules, proteins, peptides and liposome-based therapies.

Aperture Plate

Aperture Plate (enlarged 250X)

Electronic Micropump Aerosol Generation



How Is It Applied?

When incorporated into one of Aerogen's specialized nebulizer or inhaler platforms, OnQ resolves many of the challenges presented by traditional and other competing methods of pulmonary drug delivery. These proprietary platforms can be customized according to therapeutic specifications, creating novel aerosolized drug products that offer valuable clinical benefits.

Aerodose® Inhaler

Designed to provide patients who require daily therapy for chronic disease with a convenient, discreet option, the Aerodose inhaler (in development phase) utilizes OnQ to produce an aerosol for efficient delivery to either the central or deep lung. This pocket-sized inhaler incorporates breath-activation and an adjustable multi-dose container, which allow a patient to simply dial, dispense and inhale each dose of drug.

Trials using the Aerodose inhaler (clinical version) for delivery of liquid insulin demonstrated excellent dose-to-dose reproducibility compared with subcutaneous injection. Its efficiency is expected to maximize drug cost efficiencies compared with other pulmonary insulin products.

OnQ Advantages

- ***Aerosolizes a broad range of drugs in solution or suspension***
- ***Produces consistently-sized aerosol particles that can be customized for either central or deep lung delivery***
- ***Rapidly delivers a predictable and reproducible dose***
- ***Minimizes deposition in the throat and mouth***
- ***Leaves virtually no wasted drug***
- ***Operates silently (<35 dB), without generating heat or using propellants***
- ***Customizable in a range of specialized nebulizers or inhalers for acute care or home applications***
- ***Uses standard liquid pharmaceutical formulations, providing expedited time to clinic and cost advantages over dry-powder formulations***

Aeroneb® Professional Nebulizer System

The Aeroneb Pro, used in the acute care setting for treatment of respiratory disorders, represents the first significant innovation in aerosolized drug therapy in more than 20 years specifically designed for patients requiring mechanical ventilation. The product offers the potential to improve drug delivery efficiency and reduce drug and personnel costs associated with in-patient care.

Using OnQ, it emits a low-velocity aerosol that minimizes turbulence and adds no pressure or volume to closed breathing circuits. In vitro *studies indicate that the Aeroneb Pro can deliver greater than four times the amount of medication to the lungs or 13%[1] of the nominal dose, compared with delivery by conventional small volume nebulizers (1-3%)[2]. Additional* in vitro *studies using OnQ in next generation products suggest that drug deposition efficiency can exceed 60% during mechanical ventilation.[1]*

[1] Dose deposited *in vitro* at endotracheal tube. Source: Fink JB, Schmidt D, Power J. Comparison of a nebulizer using a novel aerosol generator with a standard ultrasonic nebulizer designed for use during mechanical ventilation. ATS 97th International Conference, May 2001.
[2] CJ Harvey et al. Eur Respir J 1997; 10:905-909.

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Efficient pulmonary drug delivery. On target, every time.

Pulmonary drug delivery is a standard of care for treatment of respiratory diseases and a viable option for systemic delivery of drugs typically requiring administration by injection. The lung's central and alveolar epithelium is ideally suited for drug deposition and absorption with over 1,000 square feet of surface area. However, achieving efficient aerosol delivery into the lungs is a formidable challenge that has hindered development of novel aerosolized drug therapies, particularly for patients in the acute care setting.

Aerogen's OnQ™ aerosol generator sets a new performance standard for pulmonary drug delivery by efficiently delivering aerosolized drugs to the lungs, on target, every time. OnQ produces a fine liquid mist of precisely defined particle sizes that can be tailored for respiratory therapy or systemic delivery, and is capable of delivering a broad range of drugs in solution or suspension.

When OnQ is incorporated into Aerogen's specialized nebulizers or inhaler platforms, the opportunities for creating improved therapies are almost limitless...

(Actual Size)

How Does It Perform?

FIGURE 1: OnQ performance in the Aeroneb Pro[1]

The Aeroneb Pro overcomes the issue of inefficient aerosol delivery during mechanical ventilation, depositing up to four times more medication during simulated mechanical ventilation than small volume jet nebulizers.

	MMAD[2]	GSD[3]	FPF[4] (<5μm)	Residual Vol. (mL)[5]	Adult % Dose Deposited[6]
Aeroneb Pro Nebulizer System	2.1	2.2	83%	0.3 mL	13%

[1] Nebulization, 3 mL of 0.083% albuterol; [2] MMAD: Mass Median Aerodynamic Diameter (micrometers); [3] GSD: Geometric Standard Deviation; [4] FPF: Fine Particle Fraction; [5] Data on file at Aerogen, Inc.; [6] Dose deposited *in vitro* at endotracheal tube; Source: Fink JB, Schmidt D, Power J. Comparison of a nebulizer using a novel aerosol generator with a standard ultrasonic nebulizer designed for use during mechanical ventilation, ATS 2001.

FIGURE 2: OnQ performance aerosolizing suspensions

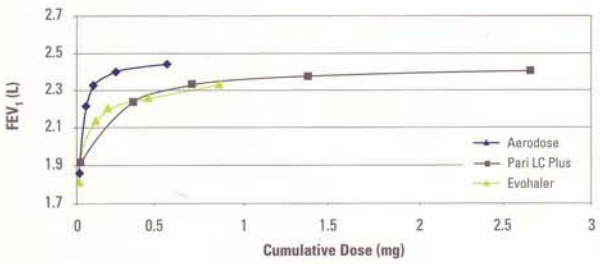
OnQ aerosol generator can aerosolize suspensions as well as or better than reported for the leading pneumatic jet nebulizer. *In vitro* testing of the Aerodose inhaler (clinical version) resulted in more than four times the respirable mass than that of the Pari LC Plus™.

	MMAD (μm)	Inhaled Drug (% of Nominal Dose)
Aerodose Inhaler	3.3 ±1.2	52.9 ±5.9
Pari LC Plus	4.8 ±0.3	15.1 ±2.4

Source: Budesonide Administration with a Novel Aerosol Generator: An *In Vitro* Evaluation. Fink JB, Simon M, Klimowicz M, Uster PS, ATS 97th International Conference, May 2001.

FIGURE 3: OnQ in the Aerodose inhaler (clinical version) vs. conventional respiratory delivery devices

The Aerodose inhaler (clinical version), using one-tenth to one-fifth of a standard single 3mL dose of 0.083% albuterol provides comparable bronchodilation to the Pari LC Plus™ jet nebulizer using a full 3mL dose in moderate to severe asthmatic patients.



Source: Albuterol Dose Response Via a Novel Dosimetric Aerodose Inhaler, Pari LC Plus Nebulizer, and HFA Ventolin Evohaler pMDI In Moderate to Severe Asthmatic Patients. Lipworth BJ, Sims EJ, Currie G, Fowler S, Coutie W, Orr L, Fishman R, Shapiro D, Taylor K., Chest, submitted.

FIGURE 4: OnQ in the Aerodose inhaler (clinical version) for delivery of inhaled insulin

Dose-to-dose reproducibility is a crucial component of insulin therapy. A head-to-head comparison of replicate doses of subcutaneously injected insulin (SC) and insulin administered via the Aerodose inhaler (INH) showed statistically indistinguishable dose reproducibility for inhaled vs. injected insulin in Type 2 diabetic patients. Peak serum insulin levels and associated metabolic effects were attained more rapidly with inhaled insulin than with subcutaneous injection.

FIGURE 4.1: Serum Insulin Levels

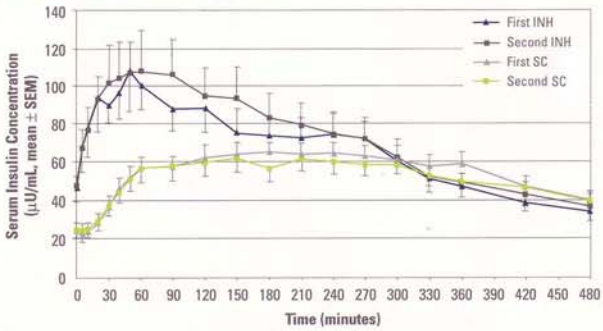


FIGURE 4.2: Glucose Infusion Rate (30 Minute Averages)

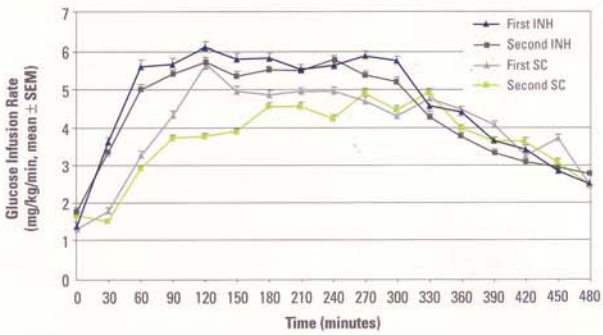


FIGURE 4.3: Summary of Intrapatient Variability

	Group means ± SD		Intrapatient CV (%)		
	INH	SC	INH	SC	p
INSULIN					
AUC0-3 (mU,mL^{-1},min)	12.2 ±8.2	4.9 ±2.1	19	23	NS
AUC0-8 (mU,mL^{-1},min)	22.0 ±13.7	13.7 ±3.8	22	16	NS
GIR					
AUC0-3 (g/kg)	0.7 ±0.3	0.4 ±0.2	19	22	NS
AUC0-8 (mU,mL-1,min)	1.7 ±0.5	1.3 ±0.4	21	19	NS

Source: Reproducibility of Inhaled and Subcutaneous Insulin in Type 2 Diabetic Patients. Perera AD, Kapitza C, Nosek L, Heinemann LW, Fishman, RS, Shapiro DA, Heise TC. Diabetes Care 2002; 25(12): 2276-81.

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