**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.
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% of the nominal dose, compared with delivery by conventional small volume nebulizers (1-3%). Additional in vitro studies using OnQ in next generation products suggest that drug deposition efficiency can exceed 60% during mechanical ventilation.1


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...
**How Does It Perform?**

**FIGURE 1: OnQ performance in the Aeroneb Pro**

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

<table>
<thead>
<tr>
<th>Aeroneb Pro Nebulizer System</th>
<th>MMAD</th>
<th>GSD</th>
<th>FPF</th>
<th>Residual Vol.</th>
<th>Adult % Dose Deposited</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2.1</td>
<td>2.2</td>
<td>83%</td>
<td>0.3 mL</td>
<td>13%</td>
</tr>
</tbody>
</table>


**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™.

<table>
<thead>
<tr>
<th>Inhaled Drug (% of Nominal Dose)</th>
<th>MMAD (µm)</th>
<th>Inhaled Drug (% of Nominal Dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aerodose Inhaler</td>
<td>3.3 ±1.2</td>
<td>52.9 ±5.9</td>
</tr>
<tr>
<td>Pari LC Plus</td>
<td>4.8 ±0.3</td>
<td>15.1 ±2.4</td>
</tr>
</tbody>
</table>


**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.

**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**

<table>
<thead>
<tr>
<th>INSULIN</th>
<th>Group mean ± SD</th>
<th>Intrapatient CV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>INH</td>
<td>SC</td>
<td>INH SC p</td>
</tr>
<tr>
<td>AUCD-3</td>
<td>(mU/mL-1.min)</td>
<td>12.2 ±8.2</td>
</tr>
<tr>
<td>AUCD-8</td>
<td>(mU/mL-1.min)</td>
<td>22.0 ±13.7</td>
</tr>
<tr>
<td>GIR</td>
<td></td>
<td>0.7 ±0.3</td>
</tr>
<tr>
<td>AUCD-4</td>
<td>(mU/mL-1.min)</td>
<td>1.7 ±0.5</td>
</tr>
</tbody>
</table>


Aerogen, Inc. 2071 Stierlin Court Mountain View, CA 94043 www.aerogen.com

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