MEDI NUCLEAR CORPORATION, INC

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An Overview of Jet Nebulizer Design, Testing and Use

Jet nebulizers have been in use for multiple decades. Throughout these decades there has been little in the way of improvement and innovation. We have seen the development of breath-assisted nebulizers and breath-actuated nebulizers, but little attention has been paid to particle size and distribution. Knowledge of particle size is essential to determining which nebulizer is best suited to deliver medication to its desired destination. Unfortunately, advances in determining particle size have been largely illusory.

Initially, particle size was determined by using technology developed for atmospheric testing, i.e.; the Anderson cascade impactor. Next came the use of lasers. Laser particle sizing depends on software and its ability to follow a given particle. It is entirely possible to generate particle sizes even in the absence of particles just with electronic noise. Even assuming these devices work as designed, they have a finite limit below which they cannot directly observe particles. This leads to artificially elevated particle sizes.

Medi/Nuclear® Corp. and Healthline® Medical utilize a cascade impactor which can observe particles as small as 0.14µ. The previously mentioned devices are virtually useless below 0.5µ. The device we use is the PC-2 Quartz Crystal 10 Stage Microbalance Cascade Analyzer, manufactured by California Measurements of Sierra Madre, CA. This is the only device purposely designed for pharmaceutical use. In the 28+ years we have been using this device, we have seen amazing reproducibility. Because of this instrument we have been able to design nebulizers of differing particle sizes to target specific areas of the lung. We have also tested most of the other nebulizers on the market and have found there is very little difference from one to the other.

It has been our contention for many years that any jet nebulizer will generate a similar range of particle sizes unless something has been done to alter the particle size. Generally, MMAD's can be increased by slowing the particle stream as it reaches an impact point, but increasing the speed of impact does little to decrease the MMAD. Particles are similar simply because accelerating a stream of liquid and impacting against of fixed surface will shatter the liquid into a heterogeneous mist that is related to speed and viscosity more than anything else. To have a significant effect on the MMAD, one must alter the behavior of the particle mist **after** its initial production. The most reasonable way to achieve a reduction in particle size is to insert a baffle or a series of baffles between the impact point and the nebulizer exit.

Furthermore, once the desired particle size has been achieved, it has to be delivered to the patient. Since nearly all drugs that are suitable to nebulization are salt based, humidity control is essential. Because salt is hygroscopic, any increase in humidity will cause the particles to increase in size. It has been demonstrated that this increase can be greater than 100%. Because there is no way to control humidity within the patient, control must be maintained right up to the point where the particle enters the patient.

Nebulizers and nebulizer systems produced by Medi/Nuclear® and Healthline® Medical have been designed to produce particles in particular size ranges and because of the use of unidirectional delivery devices maintain the desired particle size right up to the point where they enter the patient.

It was long assumed that the ideal particle size for delivery to the lungs was 3µ to 5µ and particles less than 0.5µ would be exhaled. More recent studies have indicated that the ideal particle size should be 1µ to 3µ. It is still assumed that particles less than 0.5µ will be exhaled.

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The fallacy of this assumption has long been demonstrated by the Nuclear Lung Scan. Scan quality has increased along with reductions in particle size. The Medi/Nuclear® NEB-3A+ Nebulizer produces particles with an MMAD of 0.28µ and well over 95% of the particles under 1µ.

We have tested many of the nebulizers currently on the market both standard, breath-assisted and breath-actuated, and have found virtually all have MMAD's near 1µ. Their package inserts and literature all indicate particle sizes of 2µ to 5µ. All have been tested with devices incapable of seeing particles under 0.5µ and thus discard information on 30 to 50% of the particles generated. Our testing is the only testing we are aware of that has tested as many nebulizers as possible under the same conditions and with the same device.

Ross Potter, Technical Director, Medi/Nuclear® Corp. Inc. and Healthline® Medical

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