



Executive Summary of White Paper on Acoustic Airway Clearance with the Frequencer™ - Clinical Evidence and Markets

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1 Summary

The prevalence of airway clearance disorders is enormous. In addition to significant quality of life issues and burden on the health care system, life-threatening situations and death may arise when the clearance of mucus from airways is ineffective. Dymedso's Frequencer™ is a novel device that uses acoustic waves to cause the lungs to vibrate and the viscosity of mucus to decrease, making it more liquid and easier to expectorate. It is superior to standard airway clearance therapy, controlling exacerbations and reducing infections and hospitalizations. The device has a large role to play in decreasing the immense suffering and fatalities related to airway clearance disorders.

2 Airway Clearance Disorders & Treatment

Disease processes can impair airway ciliary function, alter mucus secretion production and mucus rheology (i.e., making it thicker), and interfere with the cough reflex. As a whole, these are referred to as airway clearance disorders. Failure to clear secretions allows microbes and particles to collect in them, and rather than protecting the host, an environment where pathogens are protected and able to proliferate is created, resulting in a vicious cycle of inflammation and infection (i.e., chronic lung infection).

Cystic fibrosis (CF), chronic obstructive pulmonary disease (COPD), asthma and bronchiectasis alter the production and composition of mucus and function of the cilia. Primary ciliary dyskinesia (PCD), the aging process, tobacco use and other environmental toxins reduce the efficacy of ciliary structure and function. Progressive neuromuscular degenerative disorders (NMDs) inhibit the normal cough reflex. Last, but not least, acute respiratory infections such as pneumonia, influenza and novel viruses (SARS, MERS, COVID-19) can cause serious inflammation to the respiratory system and damage the cilia, resulting in severe respiratory distress requiring mobilization of secretions.

Chest physiotherapy (CPT; i.e., clapping) has been the cornerstone of airway clearance therapy (ACT). Other standard therapies include high frequency chest wall compression (i.e., Vest therapy) and positive expiratory pressure (PEP) (i.e., Acapella, Flutter, Cornet, Aerobika).

However, these therapies are mechanical in nature, and have many limitations. For example, clapping, the “gold standard”, is demanding, energy draining, can be extremely painful for the patient and can lead to rib cage fractures in the elderly and patients with osteoporosis. Furthermore, it is contraindicated for babies, pregnant women and individuals with artificial airways or who have undergone recent surgery. Vest therapy has been reported to cause pain, chest tightness, chest restriction, migraines and a feeling of claustrophobia, and cannot be used in babies or in patients with artificial airways. PEP devices are often ineffective at clearing the airways, are awkward and difficult to hold for an entire treatment, and cannot be used in neonates or the paediatric population.

3 The FREQUENCER™ – Acoustic Airway Clearance Treatment

The Frequencer was developed as an innovative solution for ACT by promoting bronchial drainage with acoustic waves at an optimized frequency that easily travels through the chest, causing the lungs to vibrate and the viscosity of mucus to decrease, making it more liquid and easier to expectorate. Mechanical waves cause strong surface effects but diminish rapidly with distance travelled into the chest. While acoustic waves are weaker at the surface, they penetrate the chest wall more easily than mechanical waves due to their ability to propagate through air and water.

The Frequencer is non-invasive and digitally controlled, consisting of a control unit and a transducer. The transducer is a disc like device that is manually applied to the front of the chest. The user adjusts the frequency of the transducer such that it causes a sympathetic resonance felt by the patient within the thorax. It can be positioned selectively on different areas, particularly the low lung areas, with no discomfort or pain. Furthermore, delivery of the treatment is always consistent.

The Frequencer matches human lung resonance frequency of ~37-42 Hz, and Dymedso has validated that repetitive sound waves at 40 Hz is the optimal frequency to reduce the viscosity of mucus^{1,2}. Clinical data^{1,3}, case studies and testimonials (> 50 case studies and testimonials in > 30 centers in the US and Canada) prove that these vibrations at the chest wall are effective and consistent at clearing pulmonary secretions in every age group and on a wide range of airway clearance issues. All case studies and testimonials indicate that the Frequencer is

¹ Cantin AM, Bacon M, Berthiaume Y: Mechanical airway clearance using the Frequencer electro-acoustical transducer in cystic fibrosis. *Clin Invest Med* 2006; 29 (3): 159–165.

² Schieppatia D, Germona R, Gallib F, Rigamontia MG, Stucchib M, Boffitoa DC: Influence of frequency and amplitude on the mucus viscoelasticity of the novel mechano-acoustic Frequencer. *Respiratory Medicine* 2019; 153: 52-59.

³ Vallejos TS, Kindel S, Phillips-Clar J: Evaluation of sputum production with the use of the frequencer with the adult cystic fibrosis patients. *Respiratory Care* 2010; ISSN: 0020-1324 e-ISSN: 1943-3654.

superior to other existing ACTs, with reports of easier mucus clearance and expectoration. Additionally, Physicians consistently report that no other treatment option exists and that the Frequencer has resulted in reduced infections, hospitalizations and exacerbations. A user survey also indicated high satisfaction with the device; it is convenient, painless and easy to use and allows targeted treatment to specific problematic lung areas.

4 The Market for Airway Clearance Devices

Airway clearance disorders result in millions of deaths per year and cause severe suffering for hundreds of millions more. The largest markets are highlighted. 1) Airway clearance diseases with a genetic underpinning (i.e., CF, PCD, NMDs) are relatively rare; however, cumulatively, in the US alone, ~150,000 people are affected. Simply extrapolating to the world's population, this results in a prevalence of 3.4M cases. 2) The prevalence of COPD (251M) and asthma (235 to 339M) is extremely high, and is increasing. Individuals with severe COPD (~65M) and severe asthma (~34M) are candidates for a device such as the Frequencer; totaling 100M cases worldwide. 3) Respiratory infections result in more than 4M deaths annually. If one considers those hospitalized or with severe cases of pneumonia and influenza, an annual total market of 16 to 30M results. Additionally, there is critical and immediate need for simple and effective airway clearance devices in the untold numbers of hospitalized COVID-19 patients. 4) There are 15M pre-term births per year worldwide, with ~1M deaths. Three-quarters of preterm deaths (750,000) could be prevented with current, cost-effective interventions. Taking the above numbers into consideration, very conservative estimates indicate that the total global addressable market is between 120 and 134M devices. Many airway clearance conditions are under-diagnosed and under-treated, especially in low and middle-income countries, and the prevalence is likely to increase due to the global shift in aging, tobacco use, air pollution and climate change. It is expected that the market will grow exponentially.

5 Conclusions

The Frequencer is a powerful tool to prevent suffering, hospitalizations, infections and fatalities related to airway clearance disorders. The Frequencer is the only ACT on the market that uses acoustic waves to cause the lungs to vibrate and the viscosity of mucus to decrease. Mechanism, efficacy and practical utility of the device have been validated in a large number of *in vitro* and clinical situations. Additionally, real-world use on a wide range of patient populations and settings shows that the Frequencer offers many benefits over standard ACT including consistency, convenience, comfort, ease of use, targeting of specific problematic lung areas, and overall increase in patient compliance. Significant markets include CF, COPD, asthma, PCD, NMDs, acute respiratory infections and pre-term / critically ill neonates. Very conservative estimates indicate that the total global addressable market is between 120 and 134M devices.