Despite a general acceptance within the industry of the superiority of pulmonary drug delivery, the delivery of drugs via the lung is currently still massively under-exploited – both for respiratory diseases and for systemic delivery.

This is largely because of the delivery issues associated with the current delivery systems that are predominantly dry-powder based. Pfizer’s Exubera was promised to herald in the next-generation dry-powder delivery technology – more than US$1 billion was reportedly written off when this project was abandoned.

Although hundreds of millions of dollars have been and continue to be spent on dry-powder delivery applications, the versatile and effective multi-drug pulmonary delivery device has to date eluded development. One of the reasons that this is believed to be the case is that there has been such a great focus on dry-powder systems. This is despite the knowledge that the lung is naturally designed to deal with moisture or liquid (humidity), and not powder (dust) which its natural inbuilt defences are structured to reject.

A new development being commercialised by Australian based Stirling Products Limited is positioned as a potential industry breakthrough. This small life sciences company is in the process of commercialising a delivery platform that overcomes the major problems of pulmonary drug delivery.

**HDA DRUG DELIVERY - A MAJOR BREAKTHROUGH**

The High Density Aerosol (HDA) platform technology (see Figure 1) introduces a new class of aerosol-generation device that is suited for use in a wide range of applications. It offers a highly effective method of delivering a diverse range of traditional pharmaceutical and biotechnology agents including both respiratory and non-respiratory drugs.

This HDA technology has proven it is highly efficient in delivering respiratory drugs such as albuterol sulphate. Additionally, where other technologies have failed, research also shows this new HDA technology is effective in delivering drugs such as insulin and pain relief medication via the respiratory route.

A recent clinical study published in the Journal of Sexual Medicine demonstrated that HDA technology was highly effective in delivering vardenafil hydrochloride. Using just a fraction of the normal tablet dose, the HDA technology reached the same plasma concentrations much faster and with less variability.

This HDA technology offers major opportunities for drug development and can effectively provide for the equivalent of the extension of patent life for existing agents merely by uniquely being able to provide for similar benefit with far lower-dose formulations.

![Mr Peter Boonen](image)

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HDA - A NEW PULMONARY DRUG DELIVERY PLATFORM CAN PROVIDE FOR MORE EFFICIENT AND SAFER DELIVERY

In this article, Peter Boonen, Managing Director, Stirling Products Limited, introduces the High Density Aerosol (HDA) Delivery Platform, a fully patented pocket nebuliser with a new ultrasonic aerosol-generating device. He describes the system’s advantages over dry-powder devices and conventional nebulisers, clinical trial results in the delivery of respiratory and non-respiratory drugs, and improved safety compared with oral administration.
ADVANTAGES OF HDA TECHNOLOGY

The HDA Nebuliser delivers at least three times the aerosol concentration of conventional ultrasonic devices (see Figure 2) and, unlike dry-powder inhalers, the HDA Nebuliser delivers the drug to the deep lung in a dissolved state with much faster absorption and much lower transportation losses. This technology represents a new class of drug delivery device offering multiple advantages over existing technologies.

These advantages include:

- can be used for multiple drug products
- constant aerosol concentration during inhalation – matched to natural inhalation
- eliminating the need for a fan to transport aerosol to the user
- minimal residual level of the liquid to be nebulised
- negligible transportation losses of the drug on the pathway to the lungs
- true breath-activation
- suitable for all ages of patients, especially children and the chronically ill
- no moving parts - increases reliability and battery life, reduces production and maintenance costs and improves convenience in service
- low power consumption
- noiseless
- pocket size device
- disposable drug capsule - key locked
- easy to operate
- rapid delivery of drug where needed (e.g. pain relief)

These advantages and features provide for true portability and greater effectiveness through reduced weight, size, cost, power consumption, reduced velocity and patient discomfort and reduced aerosol (drug) loss during transportation. Patients can inhale normally without gagging or special training.

NATURAL DELIVERY

Drugs, or any other material, administered to the lungs are naturally subjected to active metabolic barriers throughout the delivery process. As Stirling’s HDA Delivery administration is in atomised liquid formulation, matched to natural breathing, the delivered drug largely avoids or minimises the effect of three of the major problems generally associated with pulmonary delivery of drugs – all being part of the body’s natural defence mechanisms (especially to dust or powder).

i) The mucosal escalation activated through the recognition of a foreign substance (drug), results in the drug-laden saliva being naturally swallowed – a significant problem with most dry-powder delivery.

ii) Coughing – a natural defence to the sensing of foreign substance (drug) introduction. A common problem of dry-powder administration resulting in patient’s coughing up the drug, which was intended for pulmonary delivery, and swallowing it.

iii) Within the lungs, macrophages, lymphocytes, neutrophils and mast cells can release proteases and peptidases when stimulated by introduction of any foreign substance (drug). The Stirling HDA Platform drug administered product being in the sub-5 micron range ensures that firstly, far more active product is delivered to the deep lung; and secondly, enzymatic degradation of the administered drug is thereby minimised.

In meeting the industry needs for pulmonary drug delivery HDA technology opens up new frontiers for treatment of many diseases in diverse modalities such as respiratory disorders, mass vaccination, obesity, HIV, neurology, pain relief, diabetes, oncology, osteoporosis, migraine, growth hormones anaesthesiology, sexual dysfunction, ophthalmology, ENT, nuclear medicine and wound management.

This technology is able to effectively deliver agents such as insulin, hormones, proteins, interferon, antibiotics, heparin and radio aerosols.

RESEARCH DATA

To date all testing and trials of the Stirling HDA Drug Delivery Platform technology have shown it to provide for a superior and far more versatile delivery device than other pulmonary delivery devices. In general terms the HDA Drug Delivery Platform, using encapsulated single-dose liquid drug product, can more efficiently deliver the aerosol drug product than any dry-powder dispensing device. It can produce this nebulised aerosol at much higher flow rates than any current portable nebulisers, thus reducing the time taken to administer the dose.

The technology that enables this within small portable nebulisers is fully patented.
Most importantly, HDA nebulised drug delivered to the lung will provide for far improved safety in drug administration, as far less active drug (approximately 10-15%) is required to provide the same benefit as an orally administered drug, i.e. less drug – less side effects.

Trials of HDA-delivered respiratory drugs have demonstrated it to be highly effective for the administration of the following inhalation solutions used in the study:

i) Albuterol sulphate 2.5 mg / 3 ml
ii) Cromolyn sodium 20 mg / 2 ml
iii) Ipratropium bromide 0.5 mg / 2.5 ml

Additionally comparisons of HDA Technology versus standard nebulisers showed superior performance (see Figure 2).

In a clinical trial using an HDA-administered low dose of the erectile dysfunction drug vardenafil, the authors found, “… that vardenafil HCl may be administered using the ultrasonic nebuliser to reach blood levels comparable with those produced by a vardenafil 10 mg oral tablet, faster and using less drug. The two treatments are not bioequivalent, with vardenafil absorbed and eliminated faster and with less variability using the nebuliser for drug delivery. Administration via the inhalational route was not associated with any clinically significant changes in blood pressure or heart rate, and no serious adverse events were recorded, demonstrating an acceptable safety profile”.

**HDA OPERATIONAL SUMMARY**

The HDA technology uses focused ultrasonic energy to form a fountain of liquid to be nebulised that produces an aerosol from the walls of the jet that self-propels at several meters per second up a chimney-like intake tube. Atomisation of the liquid occurs at the base of the jet inside the intake tube. The micro-particle aerosol is then transported to the user by positive dynamic pressure derived intrinsically from the kinetic energy of the jet.

The HDA technology therefore does not require any compressed gas or fan driven airflow to transport aerosol to the user. This significantly increases the aerosol concentration by both eliminating the gas/fan dilution effect and reducing the drug loss associated with aerosol condensation inside the nebulisation chamber.

**COMMERCIAL OPPORTUNITY**

The patented HDA technology offers a significant opportunity to target a multi-billion market as it can be leveraged to improve drug safety profiles and thereby permit the equivalent of new patents to the improved performance versions (subject to trial validation) of some of the world’s major drugs as they come off patent.

The fully patented HDA Technology offers companies within these fields major strategic advantages over existing competition and presents a number of highly lucrative opportunities for new drug molecules or patent extension programs.

Stirling Products Limited will be trialing its final pre-production prototypes in late 2011 and early 2012 and is interested in discussing exclusive HDA licensing opportunities with potential partners.

**REFERENCES**

Stirling Products Limited invites interested companies to partner in one or several of its leading healthcare technologies for global or regional deployment. The following summarizes our Company and key opportunities:

ABOUT Stirling Products - is an emerging global healthcare company listed on the Australian Securities Exchange (ASX:STI). Stirling can offer its potential partners unique opportunities in the healthcare device and product markets.

ABOUT TeleMedCare - through the regular, secure and remote vital signs monitoring of chronically ill patients, TeleMedCare provides an unprecedented level of care, patient peace of mind, and also saves health authorities the major expenses associated with unnecessary hospitalizations and medical visits.

ABOUT High Density Aerosol Drug Delivery — is in pre-production phase of manufacturing the world’s first commercial mass-scale small portable nebuliser capable of delivering many different drugs.

ABOUT Stirling Health — is a premier Australian pharmacy only sales and marketing business that covers all Australian pharmacies representing both agency and Stirling products.

ABOUT Stirling Pharma - owns a 4,270 sq. m. cGMP pharmaceutical facility committed to the manufacture and commercialization of prescription, over-the-counter, nutraceuticals, and natural health products.

For further information see www.stirlingproducts.net or contact:

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