Design of a dry powder inhaler

**Promoter:** Pierre Lambert (pierre.lambert@ulb.ac.be)

Co-promotors**:** Jonathan Goole (jonathan.goole@ulb.ac.be), Nathalie Wauthoz (nawautho@ulb.ac.be)

**Candidates profile:** any profile with a strong physical insight, with an interest in CAD, 3D printing, design methodology

**Problem definition**

Drugs for respiratory diseases (asthma, BPCO, bronchitis…) are typically delivered to the lungs as aerosol thanks to pressurized metered dose inhalers or dry powder inhalers (DPI). Such DPI are also used to deliver inhalable insulin (e.g. Afrezza®) for systemic delivery or antibiotics (e.g. tobi podhaler®) against lung infectious, and several new research projects already described the use of inhalable dry powder formulations in targeted therapy for lung cancer. DPI are designed to build to fulfil different essential functionalities to allow depositing a formulated dry formulation into the lungs (e.g. proper storage of the drug in an internal reservoir (reservoir, cartridge, blister) or an external capsule, aerosolisation of the loaded powder and deagglomeration system of the aerosolized powder to allow reaching the deep regions of the lungs, and a mouthpiece to guide the aerosol. Moreover, they present other functions to help the patient to be confident with its dose delivery (e.g. counting the number of delivered doses, end-product signal, dose delivery signal,…). Nowadays, a lot of different architectures of devices can be found in the market (e.g. Handihaler®, Neohaler®, Podhaler®, Aerolizer®, Novolizer®, Turbohaler®, Diskus®), each of them being designed to provide effective aerodynamic properties to allow carrying the drug to the lungs. Despite the fact that many efforts have already been made to improve the effectiveness of DPI, much work remains to be done to increase patient compliance with this type of treatment. Indeed, inhalation devices generally require several handling steps in order to administer the medicament correctly. Reducing the risk of mishandling and reducing inter- and intra-subject variability remains a topical concern.



Source: Capsugel

Therefore, many questions open the way to innovative designs in the domain: improve the turbulence of the flow towards better drug delivery; breath actuated devices embedding threshold systems to deliver the drug only when the inhalation is strong enough; adaptation (dedication) to new/specific formulated drugs; anti-adhesive coatings for the inner channels of the device; avoid the mishandling with an automated drilling system; enable the loading the bigger loaded capsule while preserving similar both aerodynamic and deposition properties.

**Goals description**

The goals of the project are to achieve a functional analysis of the available devices (how they work) and to test 3D printing of such devices. Such prototypes could be then characterized experimentally and the conclusions will serve as a basis to the definition of future developments.

**Work description**

1. **State of the art:** read and understand the working principles of dry powders inhalers presented in both the scientific (scopus) and patents literature. The goal is to provide an engineer point of view, which will complement the understanding of the pharmacists associated to the project (Prof. J. Goole and Dr N. Wauthoz);
2. **Feasibility study based on Ember 3D printing**: the first step will be to replicate an existing device, ie drawing the CAD files, running them on a 3D printing machine (Ember) and, after assembly, characterize their performances in terms of powder deposition in a Next Generation Impactor (artificial lung model)
3. **Design and optimization**: based on the obtained results, a new design will be discussed between the student and the (co-)supervisors. In this step the student will implement the design methodology. The goal is to characterize the proposed designs by combining the prototypes parameters with the working parameters mimicking the patient (suction pressure, flow rate…) to identify interesting regimes (for instance a device indifferent to “patient”).
4. **Adhesion study**: adhesion of powders on the inner walls of the device are expected to strongly depend on the wall roughness. In order to better understand these adhesion regimes (and beside a complementary literature review), the student will manufacture controlled textures surfaces with the Nanoscribe 3D printer (resolution down to 100nm) and study the adhesion of drug grains (1-5µm) and carrier lactose grains (50-100µm) with optical microscopy.

**References:**

Chan, Young, Traini, Coates, Dry powders inhalers: challenges and goals for next generation therapies, Pharmaceutical technology Europe, 19:4, pp 19-24 (2007)

Kou, Cao, Review of dry powder inhalers devices, American Pharmaceutical Review, 19:3 (2016)

Flore Depreter, Development of dry powder formulations of proteins for inhalation, PhD thesis, ULB, 2011-2012.

# Yang, Chan, Chan, Pulmonary drug delivery by powder aerosols, Journal of Controlled Release 193: pp 228-240 (2014)

And citing articles… (to be looked at on www.scopus.com)