## Reg. No: 2017/25/N/ST8/00809; Principal Investigator: mgr in . Agata Dorosz

In accordance with statistics reported by the World Health Organization, lower respiratory infections are nowadays the most deadly communicable diseases in the world. Chronic obstructive pulmonary disease caused 3.2 million deaths in 2015. As stated in the aforementioned estimates, some 235 million people currently suffer from asthma, which claimed 383 000 lives in 2015. Moreover, lung cancer (along with trachea and bronchus cancers) is the most common malignant tumor and the fifth leading cause of death globally that was responsible for 1.69 million deaths in 2015. Therefore, the awareness of threats arising from chronic respiratory diseases is a cornerstone of all efforts for further improvement of the inhalation treatment methods.

Passive Dry Powder Inhalers (DPIs) are the most marketed devices of the various pharmaceutical aerosol delivery platforms available. What renders them highly popular is the auto-synchronization of inspiration and drug release, as these breath-activated systems employ the turbulent energy derived from the inspiratory airflow to discharge and aerosolize the drug dose. The principal of operation contributes to the distinctive character of the phenomena occurring in passive DPIs. For this reason these medical devices constitute a specific subject of basic studies in the field of biomedical engineering, namely the mechanics of therapeutic aerosols.

Literature review shows that many researchers have handled the great challenge to examine dispersion, transport and deposition processes during aerosol therapy with passive DPIs. However, this task is not fulfilled straightforwadly, owing to the complexity of the process analysis. Widespread research must deal with the interplay of the powder formulation, DPI inhaler design, geometry of air passages and inhalation technique with its airflow curve. The vast majority of *in vitro* and *in silico* investigations assume inhalation of averaged, constant flow rate conditions. Nonetheless, this approach may result in a severe misunderstanding of physics of the occurring phenomena. Underestimated and disregarded, the unsteadiness of the breathing cycle is a factor difficult to investigate and its effect on aerosol mechanics during drug administration is still inadequately evaluated. This aspect underlies a scientific problem aimed to be solved by the proposed project and accounts for its pioneering nature.

The planned project concerns processes of aerosolization, transport and deposition of aerosol emitted from passive Dry Powder Inhaler (DPI). In terms of planned work a basic *in vitro* research will be conducted. The main objective of the project is to investigate how the dynamics of inspiration affect aerosol entrainment, transport and deposition events in real-time, with an unsteady airflow through DPI and human air passages. A comprehensive analysis of the aforementioned phenomena is expected to help by providing answers to the following questions:

- How do dynamics of inspiration affect the time course and the time duration of the aerosol emission process?
- How do dynamics of inspiration affect the quality of the aerosol cloud (particle size characteristics) and the distribution of the drug dose deposited in the upper and lower respiratory tract?
- How do aerodynamic conditions in the studied system affect the dispersion and deposition processes, when considering their variability in time?

In the intended research the methodology of chemical and process engineering will be applied, as it is widely used to solve biomedical problems related to optimization of aerosol therapy. The outcomes of the study will distinctly extend the current state of knowledge about particle aerodynamics, as it will allow to foresee the real behavior of aerosol particles in the aerosol flow field. Furthermore, the expected result is to provide information on maximizing the dose of the drug deposited in the desired bronchial tree regions by performing an inhalation maneuver with a suitable time course. The proposed work will substantially enrich the findings of clinical trials when drawing up guidelines for a proper inhalation technique. The planned project will also allow the acquisition of a new, basic knowledge of the studied phenomena that can play a significant role in developing innovative inhaler designs for the more effective performance.