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THE CHALLENGE TO APPROVE A GENERIC INHALATION PRODUCT IN EUROPE ACCORDING TO THE NEW OIP GUIDELINE

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In the last years many blockbuster drugs are running out of patent protection and become available for generic industry. While an approval of pharmaceuticals for absorption from the gastrointestinal tract usually only requires information on drug compounds and formulation, an inhalation product consists of a drug compound, a formulation, a delivery device and the skills and treatment compliance of the patient to use the product. The feasibility of inhalation strongly depends on the combination of these four elements. In detail pulmonary deposition which determines efficacy depends on the physical properties of the delivered aerosol (device and formulation aspect) and on the patient's use of the device (breathing pattern, breathhold). The European Medical Agency met these concerns and issued a new Guideline for orally inhaled products (OIP, 2009). This guideline considers the patient's breathing pattern and ability to use a device in a certain state of disease: "This guideline will address data required which are often dependent on the performance of the device from which the active substance is inhaled. This document will address specific issues of relevance to inhaler devices". The aim of this contribution is to demonstrate specific challenges of the approval process of an asthma and COPD dry powder combination product for inhalation (DPI). One of the main hurdles was the determination of the different flow profiles through the test and reference devices achieved by the different patient groups. The goal of the development of the product is to achieve similar performance (aerosol output rate and particle size distribution) of the test and reference product at all observed breathing patterns. It was found to be essential to get a deep understanding of the behavior of the reference product. Due to batch to batch variability and aging effect, that we found during development, it was extremely difficult to define the performance targets for the test product.The problem was solved according to the OIP guideline and by an optimization of the formulation and design of the test product. The guidance according to OIP: "At least three consecutive batches of the test product and three batches of the reference product should be tested.". This procedure should avoid a simple batch selection. In summary this example shows the complexity of the development and approval process for generic inhalation products.