CONTRIBUTE TO THE OINDP RISK MANAGEMENT MATRIX
What do you think are major CMC risks for OINDP's?

Interactive Addition to Poster:
Rationalized Approach to Chemistry, Manufacturing & Control (CMC) Requirements For Orally Inhaled and Nasal Drug Products (OINDPs) Based on Risk Management

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	Major Performance Targets			
Major Risk Categories	Reliable & Consistent Aerosolization	Excluding Unintended Materials	Encouraging Proper Use	Minimizing the Likelihood of Unintended Effects
Device	All OINDP systems require some form of energy transfer to generate the therapeutic aerosol with an aerodynamic particle size <5-7 microns. The power transfer should be consistent. The power source should be reliable and robust.	Inhalation systems are designed for deep airway deposition of therapeutic particulates and are attempting to defeat or bypass natural defense mechanisms against such deposition. It must be kept in mind that unintended foreign materials from the device can also find their way into the same airways. This is of special importance for repeatedly used long term medications.	Patient handling and use should be as obvious as possible. Avoid confusion in handling with or administration of similar devices (interchangeability); avoid likelihood of swallowing or mistakenly taken as a regular oral preparation.	Some devices that store energy (e.g. pMDI etc.) can be inadvertently activated when not intended.
Formulation (including manufacturing process)	The amount and deposition pattern of inhaled agents is dependent on the actual amount delivered from the device and the aerodynamic behavior of the produced particulates. Reproducibility in function throughout the intended use period is critical.	Microbiological risks are inflated for COPD, emphysema, and cystic fibrosis patients where the hyperproduction of mucous and reduced ability of the cilliary clearance mechanism to remove material from the airways exists.	Formulation taste can impact patient compliance (e.g. bitter tasting preparations might discourage compliant usage; lack of taste or sensation might be interpreted as dose not administered).	The health status of the lung will play a significant role in local adverse reactions or systemic exposure for any individual patient. In asthma, airway hyperreactivity can be triggered by only small amounts of an offending substance intentionally or unintentionally delivered with the formulation.
Device/Formulation Interactions	Inhaled doses are typically small but encounter large surface areas of the device component or solid excipient. Shifts in adhesion or repulsion forces between the formulation and device can lead to losses or excess release of the inhalable dose.	Extractables/leachables/volatiles (in particular, nitrosamines and polynucleararomatics [PNA]) from device contact surfaces or packaging material contact surfaces.	The spray plume geometry can be a resultant of device (e.g. actuator sump and spray orifice) and formulation (e.g. vapour pressure and evaporation rate) if too fast can make breath coordination more difficult in pMDIs for example.	An integrated dose counting device when malfunctioning has the potential to tell a patient that they have drug doses remaining when they don't.
Patient Factors	Devices using the energy of the patient to generate the aerosolised dose need to consider the peak inspiratory flow rate, inspiratory volume and rise time capabilities of the target patient population.	Microbial contamination of a device from contact with a patient during dose administration or when carried may deposit organisms to inaccessible surfaces of an inhaler that are difficult to clean.	Non-pulmonary disease that affects ability to use a device (arthritis)	Similar OINDP's from different manufacturers may, however, have entirely different use instructions that goes unrecognized by patients prescribed both products.

Post your opinions in the appropriate cell

Some examples are given to help you get started.

Can't explain it all today? Leave a business card for follow-up contact by the Risk Management Working Group