Sneak Peek

CMC and Regulatory Requirements for Inhalation Drug Products

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ONLINE
TRAINING

Nebulizer

01

Jet actuated system use compressed air

PARI: PARI BOY® Classic[1]

Vibrating mesh nebulisers use a vibrating mesh head

PARI: eFlow®rapid Mesh Nebulizer[2]

Philips: I-neb® Advance Nebulizer[3]

Vectura: FOX® Mesh Nebulizer

Ref.: 1: myhealthhillingdon.nhs.uk
2: https://www.pari.com/uk/products/inhalation-devices-for-the-lungs-uk/eflow-rapid-nebuliser-system-uk/
3:https://designawards.core77.com/Commercial-Equipment/84237/Philips-I-neb-Advance
4: https://www.vectura.com/services/device-platforms/

Nebulizer: Key Aspects & Applications

02

Nebulizer[1,2,3]			
Nebulizer Type	Device with pressurized Air for Nebulization	Membrane Nebulizer (Vibrated mesh inhaler)	„Nebulizer“, Actuation by manual power
Indications	Asthma/COPD/Pulmonary Arterial Hypertension/etc.		
Inspiration Flow Rate	15 – 30 L/min		
Drug Load	µg up to several g		
Actives	SABA/LABA/LAMA/ICS/Antibiotics/etc.		
Formulations	Aqueous solutions or suspensions		
Examples	Breelip® (Ventavis), PARI BOY® Classic, FOX® Vernebler, Pulmospay® Inhaler		

Ref.: 1: myhealthhillingdon.nhs.uk; 2: https://www.vectura.com/services/device-platforms/; 3: https://resyca.com/products/

SMI –Prefilled Syringe Inhaler PFSI®1/ Pulmospray®2

Operational principle of PFSI®[3]:

The aerolization is achieved using a spray nozzle unit, SNI (small silicone chip of 1x1 mm and ≈ 100 micro-nozzles). Mechanical power from a coiled spring forces a metered volume of drug solution through the SNI which forms a liquid jet that then breaks into small respirable droplets.

PFSI®: Reusable inhaler for prefilled syringes[3]

Key aspects and of PFSI® & Pulmospray®[4] SMI:

Metered volume:	50 µl - 1 ml
MMAD[5]:	5.1 to 6.7 µm
Formulation:	Aqueous solution
Indication:	Asthma, COPD, CF, PAH, potential for large peptides, highly sensitive biologics (mAbs, mRNA etc.)
Fine particle fraction (FPF)5:	up to ≈ 50 %
Lung deposition[5]:	> 50 %

Pulmospray® single use soft mist inhaler with Respi Lever DriveTM for manual actuation[4]

1: Recipharm; [2]: Resyca, Munich, Germany
3: https://www.recipharm.com/sites/recipharm-corp/files/recipharm/recourse/fact-sheet/PFSI-Soft-Mist-Inhaler.pdf
4: https://www.recipharm.com/sites/recipharm-corp/files/recipharm/recourse/fact-sheet/Pulmospray_Soft_Mist_Inhaler.pdf
5: B Muellinger, N A Buchmann, J Bartholomew, W de Kruif; Aerosol performance of the single-use Pulmospray™ soft mist inhaler for inhalation of high amounts of liquid formulations; 23rd ISAM, Idaho, USA, May 22-26, 2021

Nebulizers – Pros and Cons

04

Advantages	Disadvantages
Dosing using tidal (normal) breathing	Long treatment times
No coordination required	May not deliver a pre-metered dose
Suitable for all age groups	High drug wastage
Suitable in acute and critical care	Risk of microbiological contamination
Offers a wide dose range (µg to gram range)	Nebulisers poorly regulated medical devices
Suitable for inhaled biologics	Nebulisers sold indenpendently from drug product; inter-brand variability
Generally faster and less expensive to develop	

Guidelines & Pharmacopoeia General Chapters

05

U.S. Guidelines

- FDA Draft Guidance on MDI and DPI Products
- FDA Guidance Nasal Spray and Inhalation Solution, Suspension, and Spray Drug

EU Guideline

- EMA Guideline on Inhalation and Nasal Products

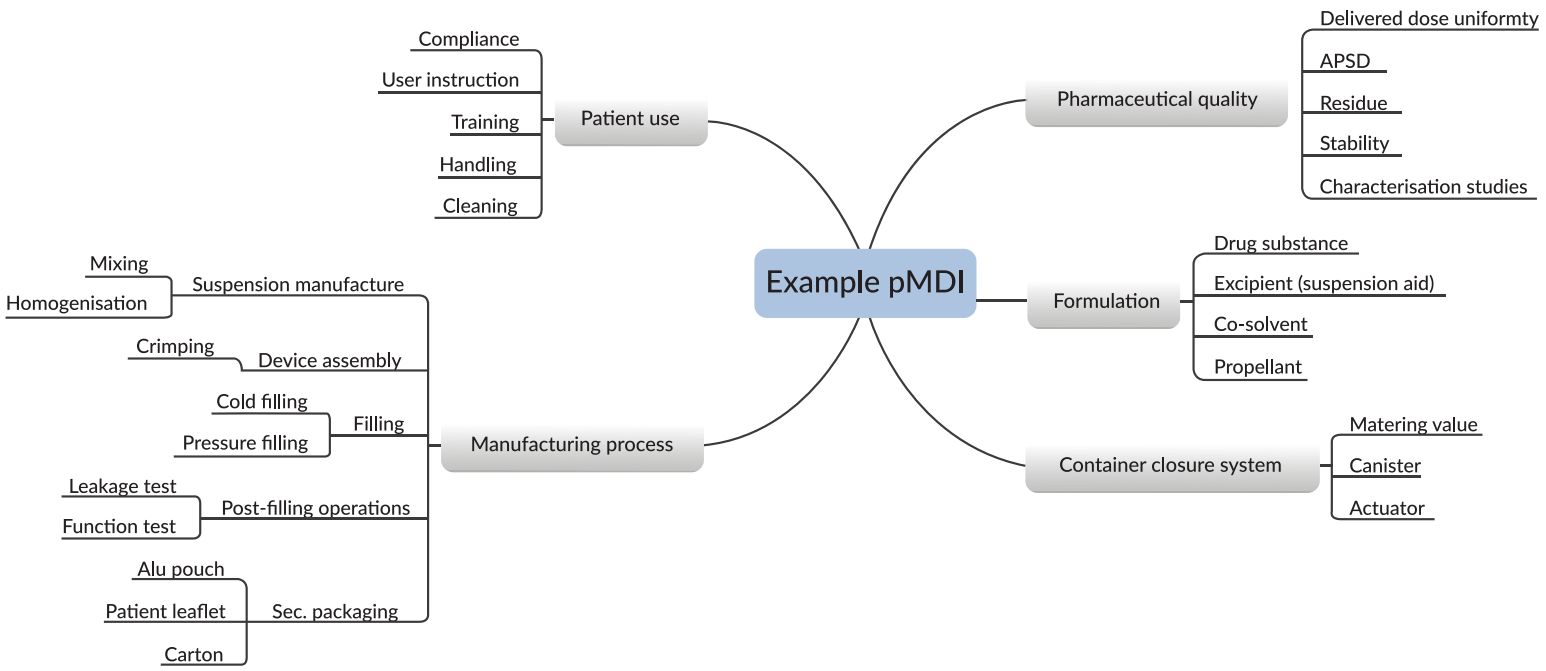
USP General Chapters

- USP <5> Inhalation and Nasal Drug Products – General Information and Product Quality Tests
- USP <601> Inhalation and Nasal Drug Products - Aerosols, Sprays, and Powders
- USP <1664.1> Orally Inhaled and Nasal Drug Products (Leachable)

EP General Chapters

- EP 0671 Preparation for Inhalation
- EP 2.9.18 Preparation for Inhalation: Aerodynamic Assessment of Fine Particles
- EP 2.9.44 Preparation for Nebulization: Characterization

pMDI: Formulation and Device Aspects



Ref.: EPAG 2010 (modified)

Registration

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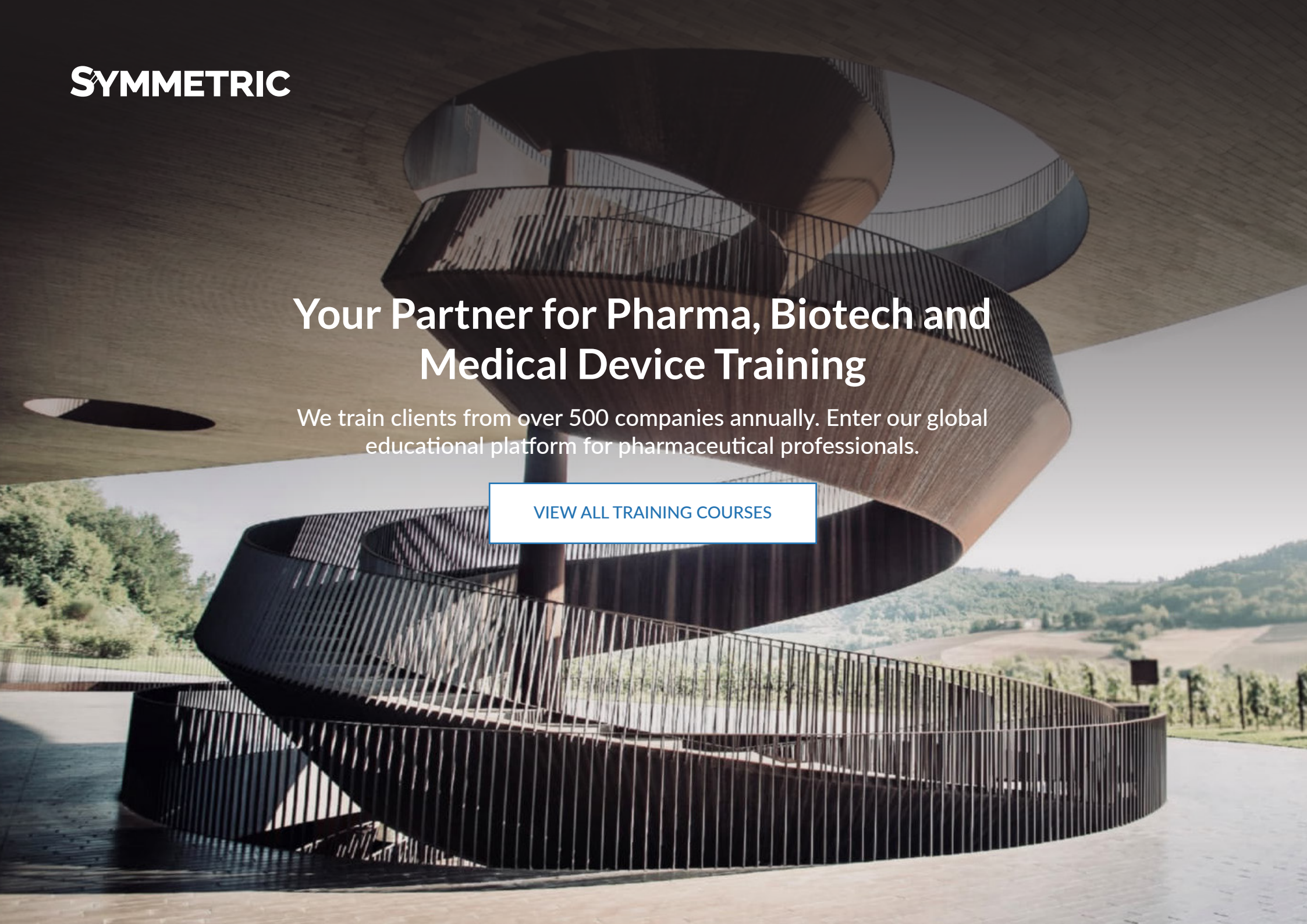
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