Assessment of Nasal Products – Proposing a New Inlet

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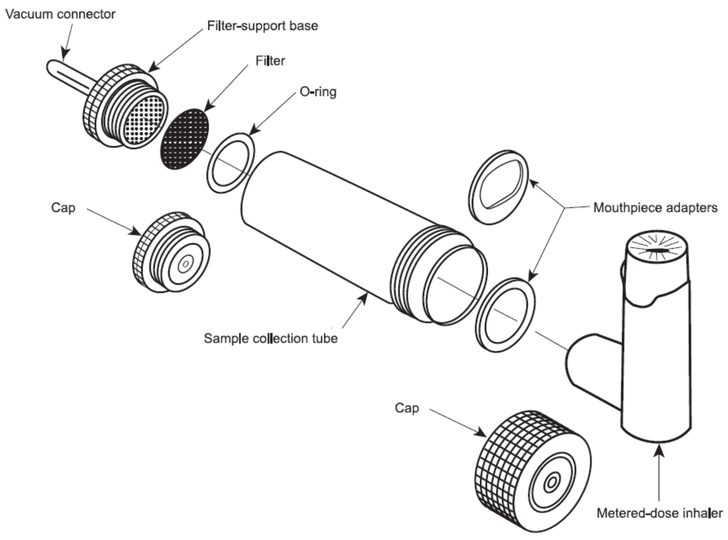
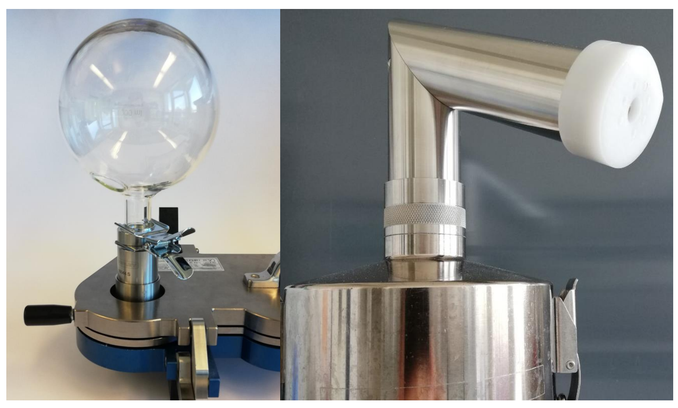
Introduction and Aim

- Increased interest in nasal application of drugs
- Regulatory requirements set by EMA and FDA, e.g., emitted dose or mass fraction below 10 µm
- Ph.Eur. proposes apparatus described in the monograph *Preparations for inhalation* for emitted dose



- Disadvantages of the Ph.Eur. apparatus, e.g.,
  - Fixed orientation of the tube
  - Unsuitable filter for high liquid volumes
  - Leakage possible

- Inlets for aerodynamic assessment like the glass expansion chamber (left) and the metal induction port (right) display similar problems



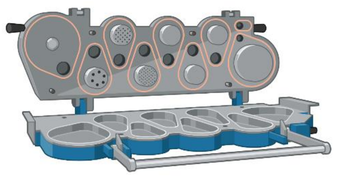
What should an ideal inlet for the assessment of nasal products look alike?

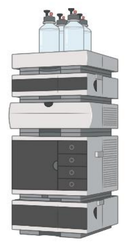
Experimental Methods

Pollicrom® (20 mg/ml solution of sodium cromoglycate)

Aerodynamic assessment

- (reduced) Next Generation Pharmaceutical Impactor (rNGI; NGI, below), Fast Screening Impactor (FSI, right)
- Standardised actuation
- 30 l/min flow rate





HPLC analysis

- RP-18 250-4 mm column
- 40% methanol, 60% 10 mM phosphate buffer (pH 2.4)
- Internal standard: salicylic acid
- Double injection

Results and Discussion

Prerequisites for optimal inlet for *in vitro* nasal product characterisation

- Operatable at 15 & 30 l/min (commonly used for nasal product assessment)
- Administration angle can be set freely to match use as in patient information
- Bypass airflow to prevent under pressure at spray nozzle and excess dose emission
- Tight sealing to avoid loss of product
- Different analytical methods possible (e.g., emitted dose, mass fraction below 10 µm)
- Applicable to all nasal products (solutions, suspensions, MDIs and powders)
- Ideally automatable analysis

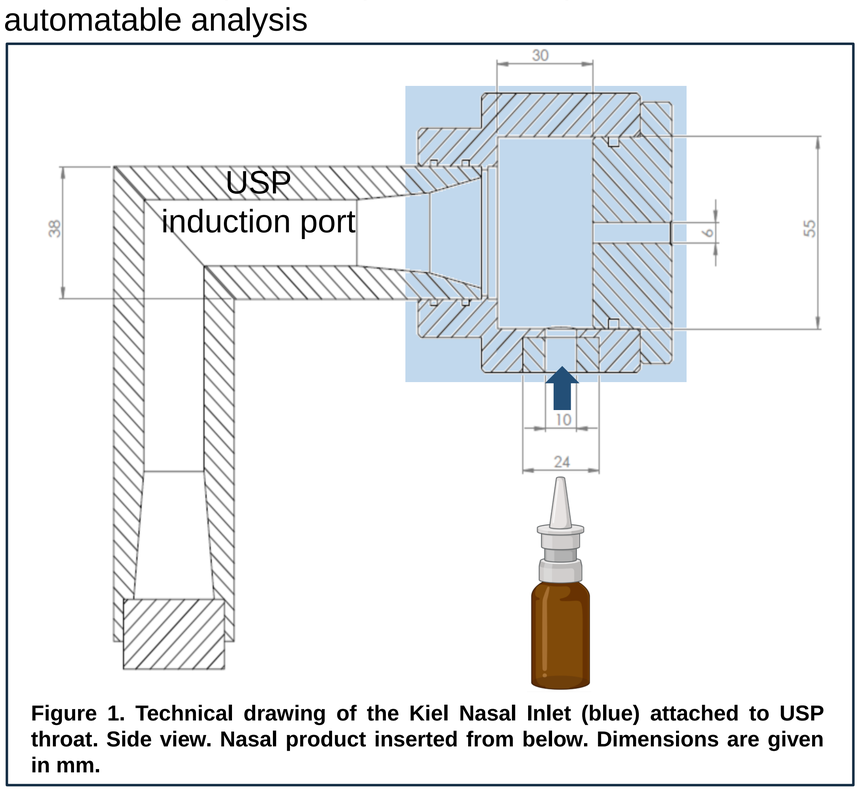


Figure 1. Technical drawing of the Kiel Nasal Inlet (blue) attached to USP throat. Side view. Nasal product inserted from below. Dimensions are given in mm.

Figure 2. Photo of the KNI with a Pollicrom® inserted. The ventilation holes visible on the right side.

Figure 3. KNI opened after one shot of Pollicrom®. Partial cloud expansion possible, no dripping visible.

Kiel Nasal Inlet (KNI)

- Moulded from rigid polyvinyl chloride
- Horizontally attached to commonly used USP induction port (Figure 1)
- Nasal product is inserted from below (Figure 2)
- Ventilation holes in the lid of the inlet (Figure 2, right) for bypass air flow
- Partial expansion of the spray cloud possible leading to impaction of droplets at the KNI ceiling (Figure 3)

Handling

- Tight sealings prevent leakage and loss of product
- No formulation leaks in between inlet components
- Geometry and material enable quick and thorough rinsing

Table 1. Assessment of the Kiel Nasal Inlet – One actuation of Pollicrom, 30 l/min. (n=3 ± SD)

Method	Mass fraction below 10 micron	Recovery	Shot mass
FSI	0.08 ± 0.01%	101.11 ± 4.71%	148.17 ± 7.09 mg
rNGI	0.05 ± 0.01%	101.24 ± 0.48%	156.60 ± 1.15 mg
NGI	0.06 ± 0.01%	99.35 ± 2.88%	156.87 ± 0.80 mg

The KNI was assessed for mass fraction below 10 µm and recovery of delivered dose (Table 1)

- Three different impactors led to comparable results
- Recovery close to 100% with acceptable standard deviation
- High recovery enables precise determination of the mass fraction < 10 µm

Conclusion & Outlook

- Kiel Nasal Inlet addresses many drawbacks of other inlets
  - Administration angle can be set freely due to exchangeable sealing
  - Leakage is prevented
  - Operatable with solutions, suspensions and powders
  - Applicable to different methods of analysis
- Further testing planned
  - Inter-lab variability
  - Determination of emitted dose with the KNI
  - Flow rate dependency
  - Influence of several spray shots on handling, recovery and mass fraction below 10 µm
  - Optimisation of setup
  - Influence of evaporation
  - Tests with other nasal products

Ideas and feedback are welcome!

Acknowledgements

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Full abstract

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