Nasal products – current and new methods for characterisation

Prof. Dr. Regina Scherließ
Kiel University, Germany

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Nasal drug delivery - opportunities

- Attractive for local and systemic delivery of drugs
  - Easily accessible
  - Non-invasive administration
  - Essentially painless
  - Good absorption
  - Rapid onset of action
  - No gastro-intestinal degradation/hepatic first-pass metabolism

- Local treatment (e.g. α-sympathomimetics, corticosteroids)
- Systemic treatment
  (e.g. desmopressin, calcitonin, fentanyl, sumatriptan, naloxone)
- Vaccination
- Nose-to-brain?

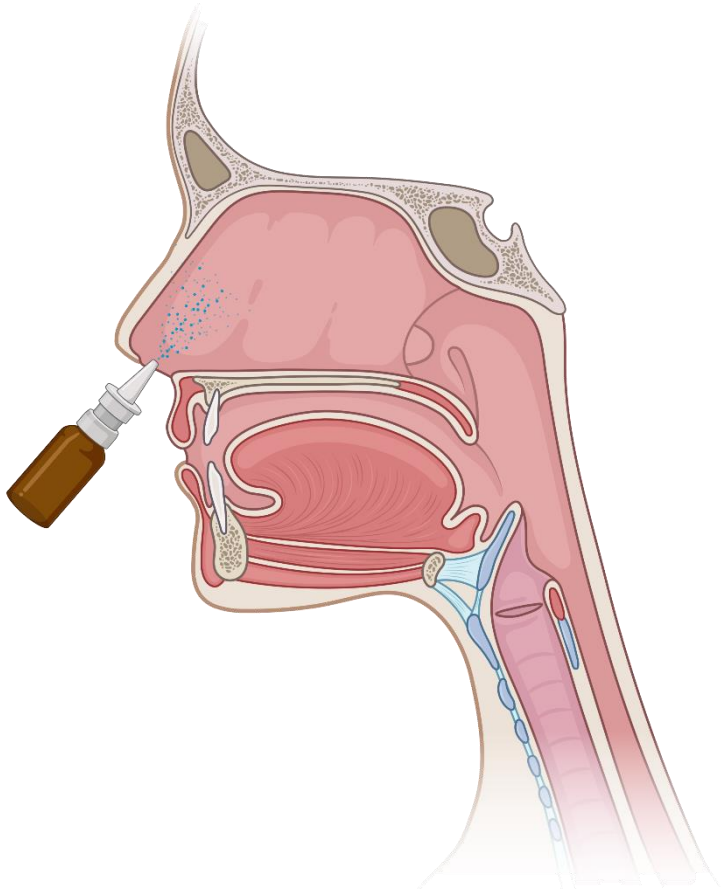
Nasal products

Nasal drops

Nasal sprays

- solution
- suspension

Nasal powders



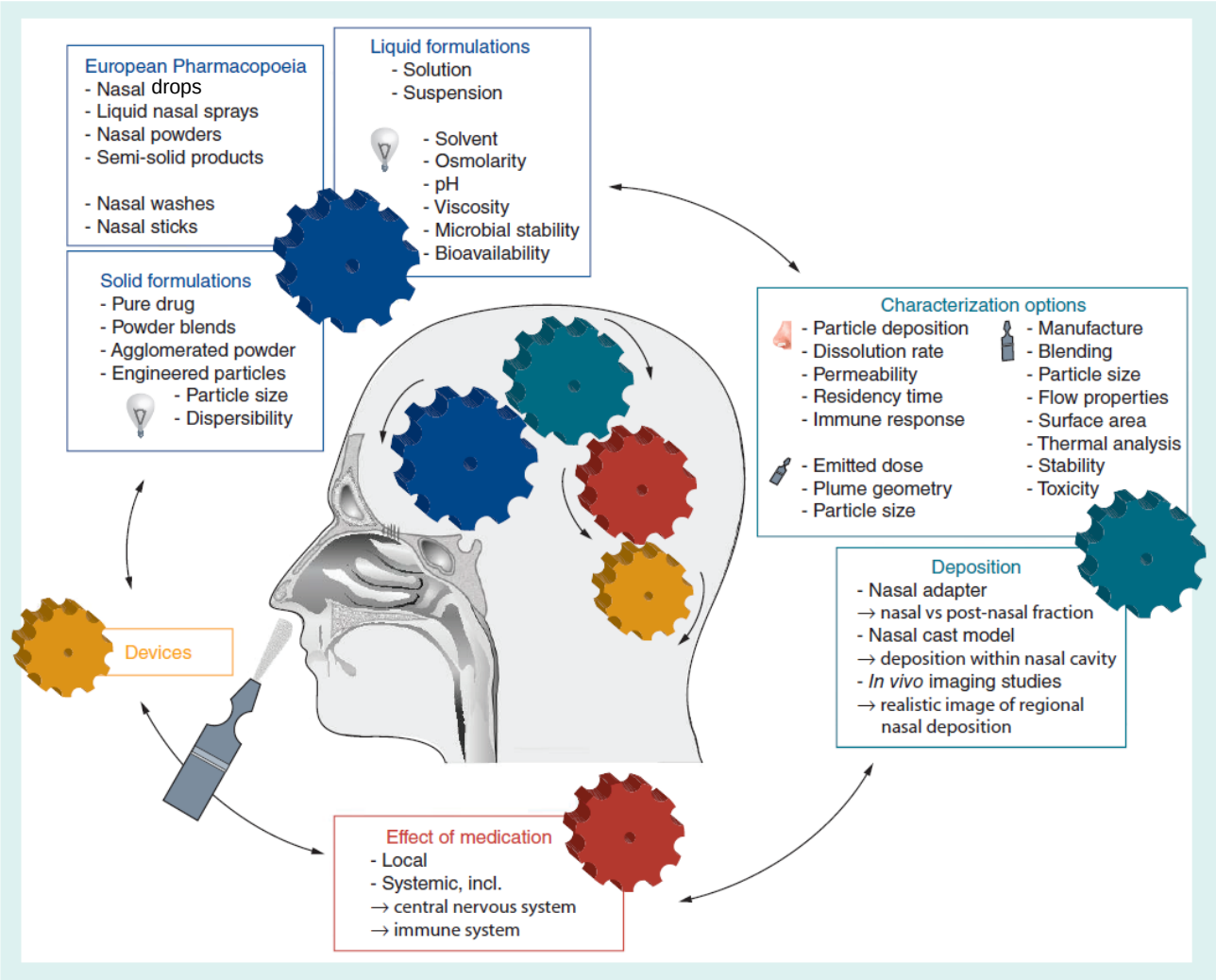
Local effect

Systemic absorption

CNS targeting

created with biorender.com

Characterisation of nasal products



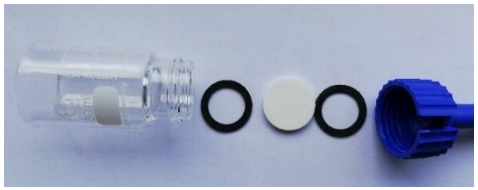
Scherließ, R., 2020. Nasal formulations for drug administration and characterisation of nasal preparations in drug delivery. Therapeutic Delivery, https://doi.org/10.4155/tde-2019-0086

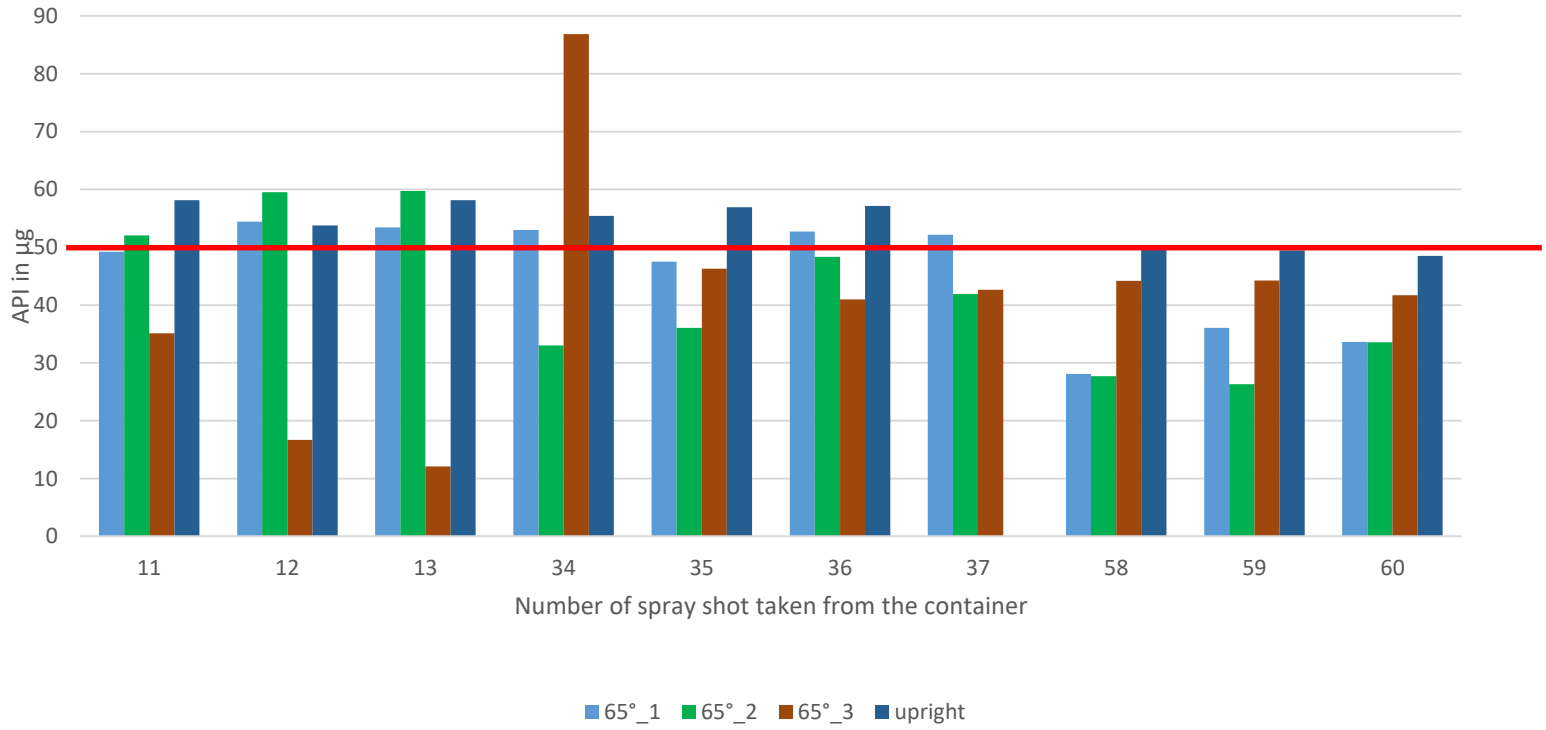
(Compendial) characterisation of nasal products

- Nasal preparations (Ph.Eur. 11.0/0676)
  - Uniformity of delivered dose
  - Number of deliveries
  - Leak rate

Delivered dose collection





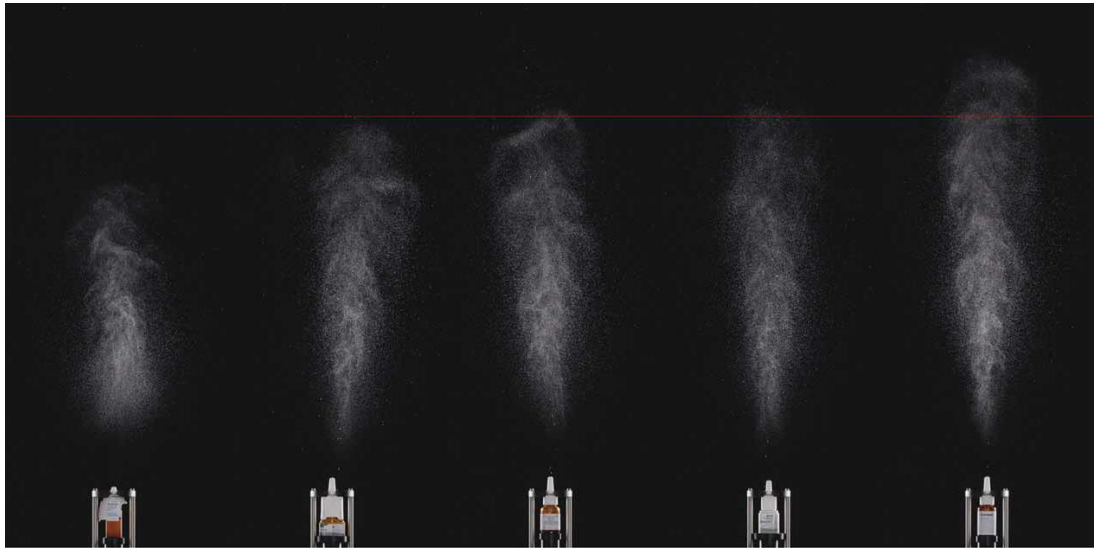
(Compendial) characterisation of nasal products

- FDA Guidance for Industry: Nasal Spray and Inhalation Solution, Suspension, and Spray Drug Products — Chemistry, Manufacturing, and Controls Documentation (2002), e.g.:
  - **pH, osmolarity, viscosity**
  - **Pump delivery, pump spray weight**
  - **Spray performance (content uniformity, plume geometry, spray pattern)**
  - **Droplet size distribution incl. percentage <10 µm**

- EMA guideline on the pharmaceutical quality of inhalation and nasal products (2006), e.g.:
  - **vast majority of the particles / droplets shall be larger than 10 microns**

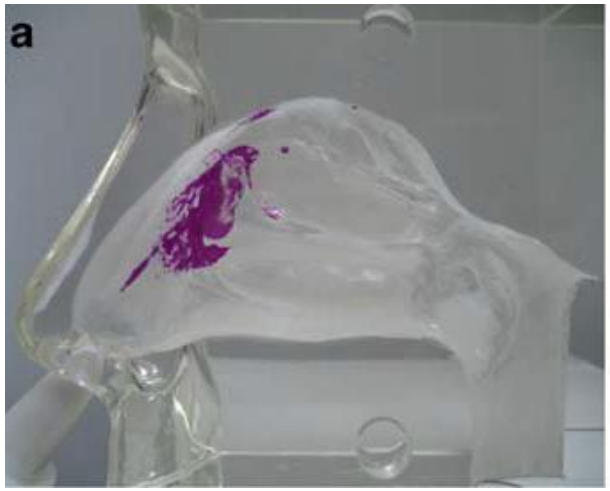
Nasal product specific tests

- Plume geometry
- Spray angle and pattern
- Deposition in a cast model

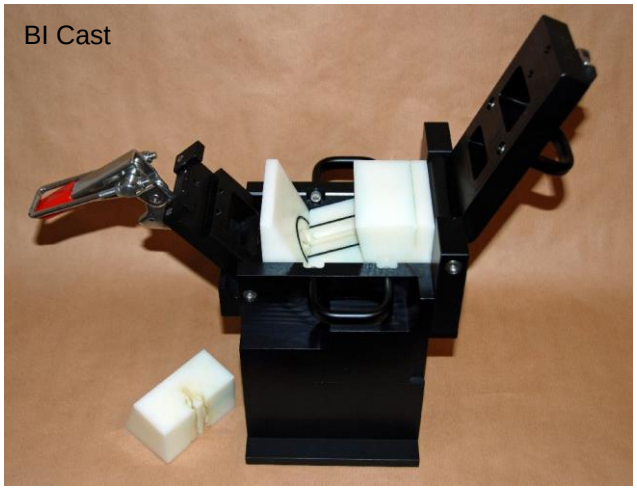


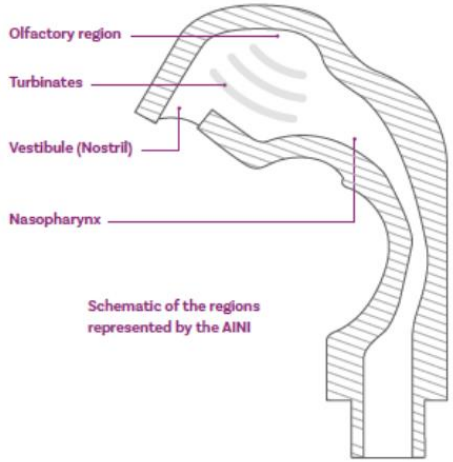
Bousquet et al. , 2015 Expert Opinion on Pharmacotherapy 16, 1-16

Regional nasal deposition - casts

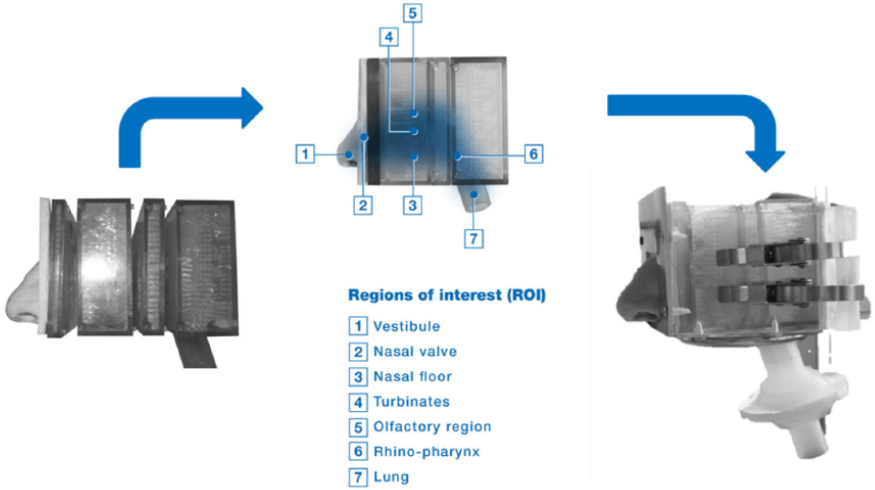


Kundoor, Dalby, 2010

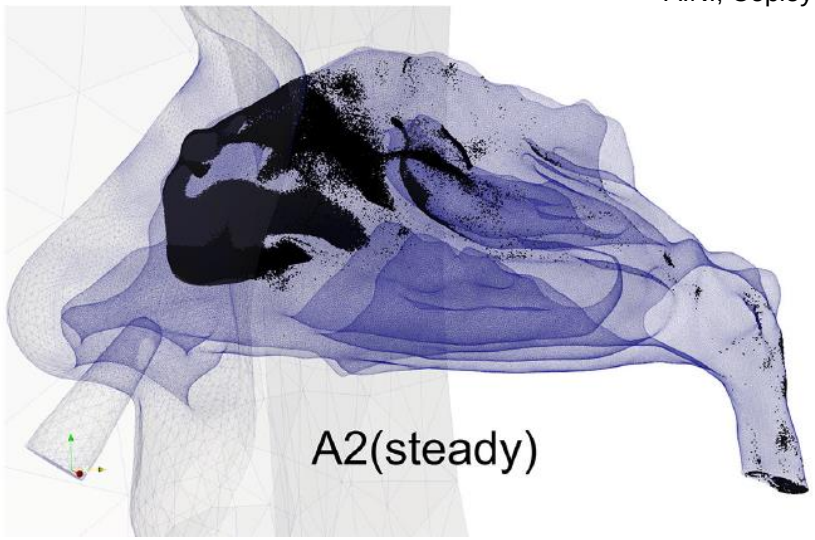




AINI, Copley

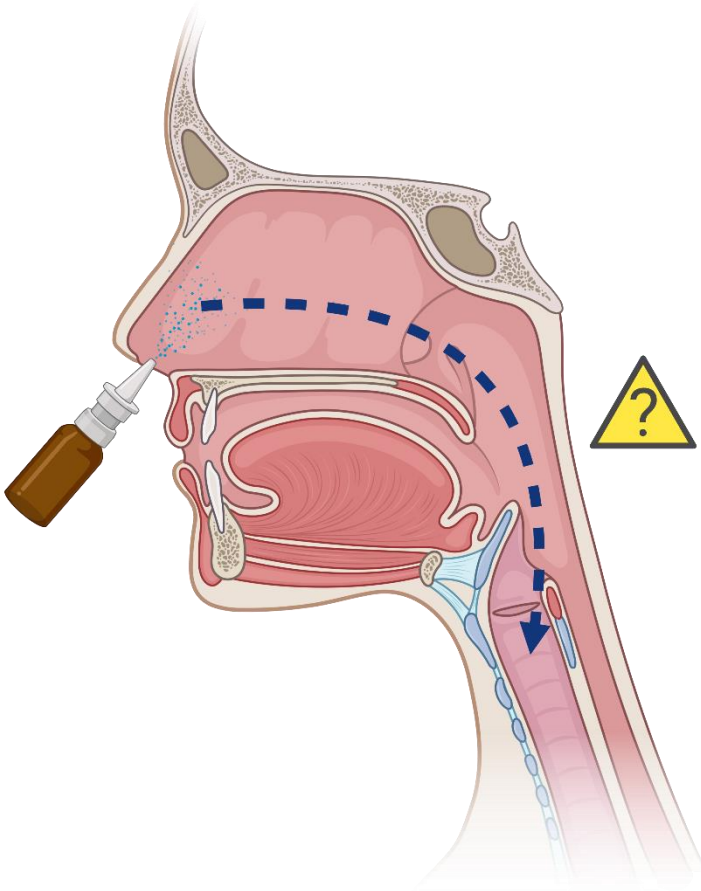


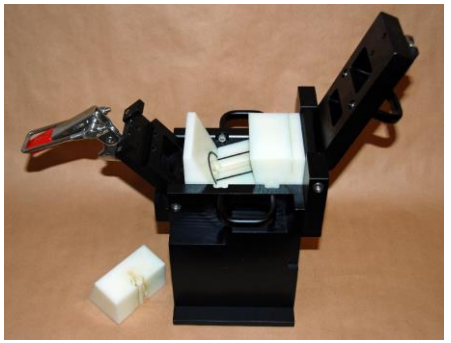
Williams & Suman 2022. Pharmaceutics, 1353

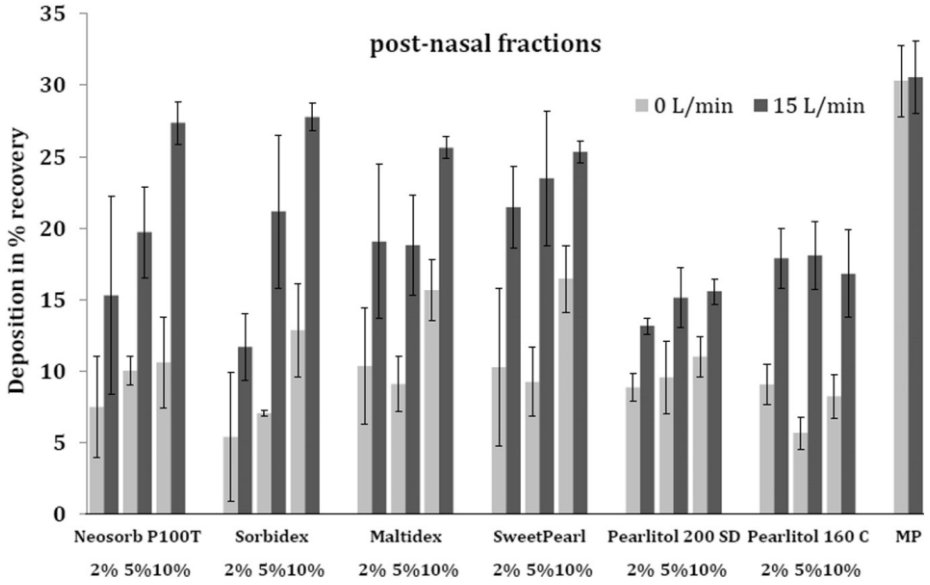


Calmet et al. 2019. PLoS ONE 14, e0221330

… pulmonary deposition?







Trows, S., Scherließ, R., 2016. Carrier-based dry powder formulation for nasal delivery of vaccines utilizing BSA as model drug Powder Technology 292, 223-231

Impactor measurements in nasal testing

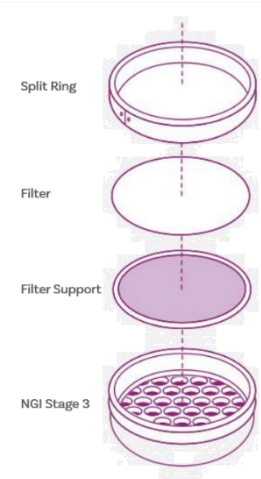
- For the quantification of **mass fraction below 10 µm**

- Prerequisites/expectations
  - Simple cut between larger 10 µm and smaller 10 µm required
  - No assessment of fine particle dose < 5 µm
  - No need for numerous particle size classes below 10 µm

  - Nasal adapter with air bypass (no vacuum/sucking from device)
  - Inlet port allowing vertical and tilted spraying (as per patient information for use)
  - Precise capture of dose (mostly liquid, > 100 µl)
  - Suitable for different products, types of products

Experimental setups

- impactors
  - FSI
  - rNGI
  - NGI
- inlet port
  - 1 L glass expansion chamber
  - metal inlet



KNI

Mass fraction < 10 µm

Poster No. 37

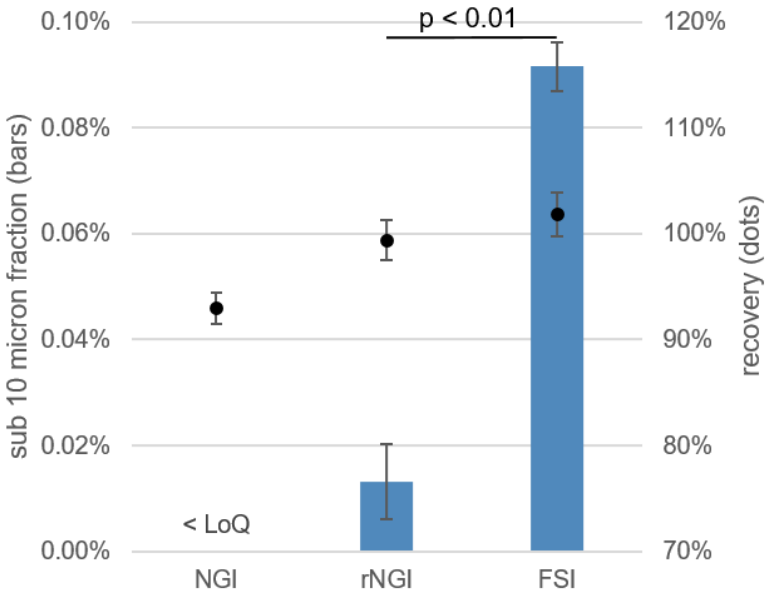


Figure 2 - Comparison of impactors. Fraction and recovery reported as percentage of determined emitted dose. Inlet: glass expansion chamber, one spray shot per assessment. (n=3, error bars=SD)

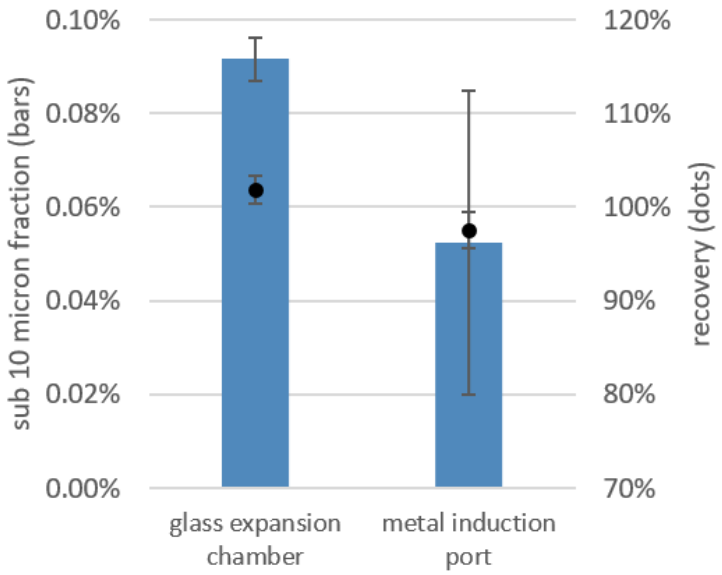
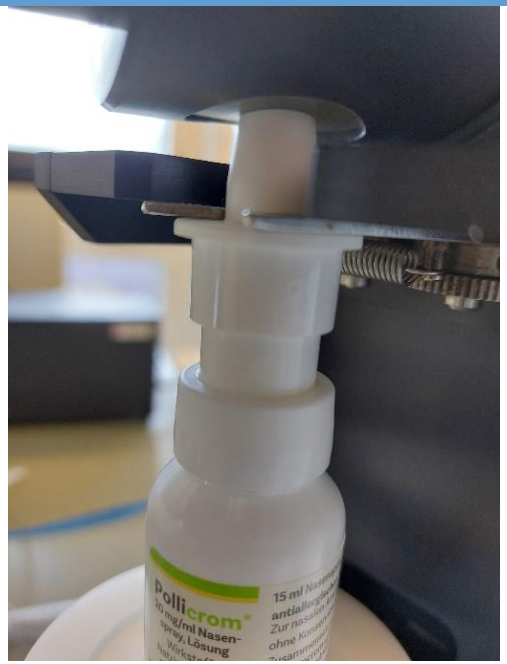


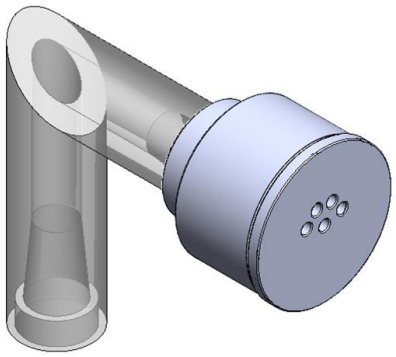
Figure 3 - Comparison of different inlets. Fraction and recovery reported as percentage of determined emitted dose. Fast screening impactor, one spray shot per assessment. (n=3, error bars=SD)

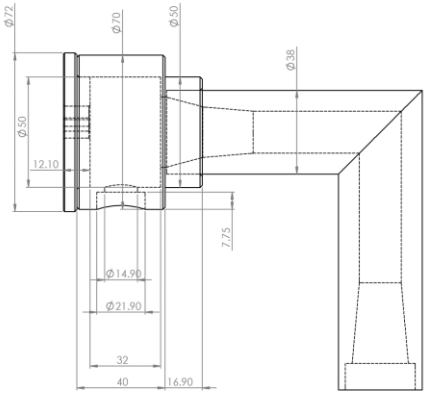
N.Baltz, R Scherließ, Drug Delivery to the Lungs, Volume 33, 2022 - Assessment of mass fraction less than 10 micron in nasal products - method considerations

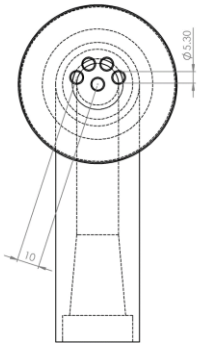
Kiel Nasal Inlet

Poster
No. 38



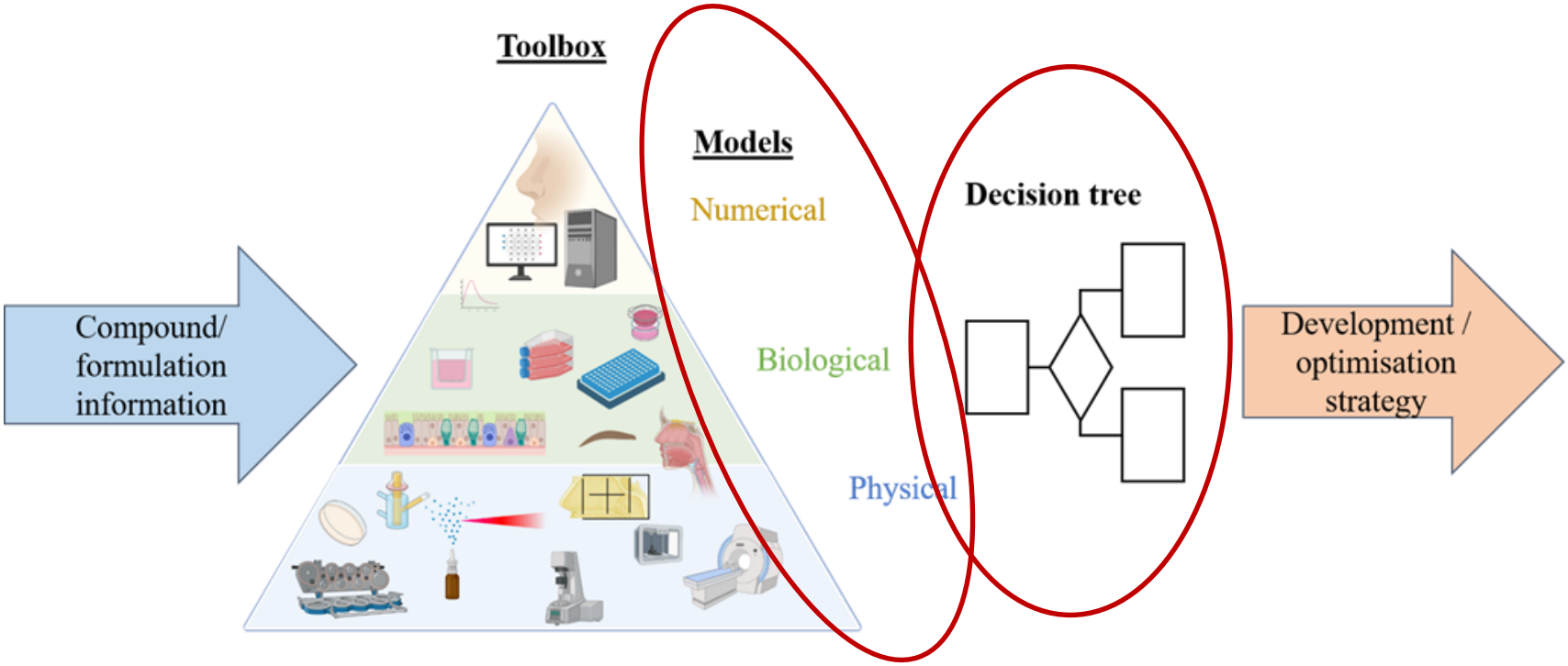






Drawings by H.Wachtel, BI

The Tech4Nose concept



MSCA DN application of CAU, KCL, UPR, UBR, ULB, BSC, LUN, NAN

Own perspective/open questions for the audience

- Current quality methods fail to account for actual use of a nasal product

- New models needed for QbD-driven development of new nasal products
- Validation across models needed

- How can nasal dose collection be standardised?
- What is the link between regional deposition and effect?
- Is a (standardised) nasal cast model useful?
- What can particle sizing tell us about effect/side effect?

Prof. Dr. Regina Scherließ
Kiel University
Department of Pharmaceutics and Biopharmaceutics
Grasweg 9a
24118 Kiel, Germany
e-mail: rscherliess@pharmazie.uni-kiel.de
phone: +49 431 880 1330