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DDL 2020
Drug Delivery to the Lungs

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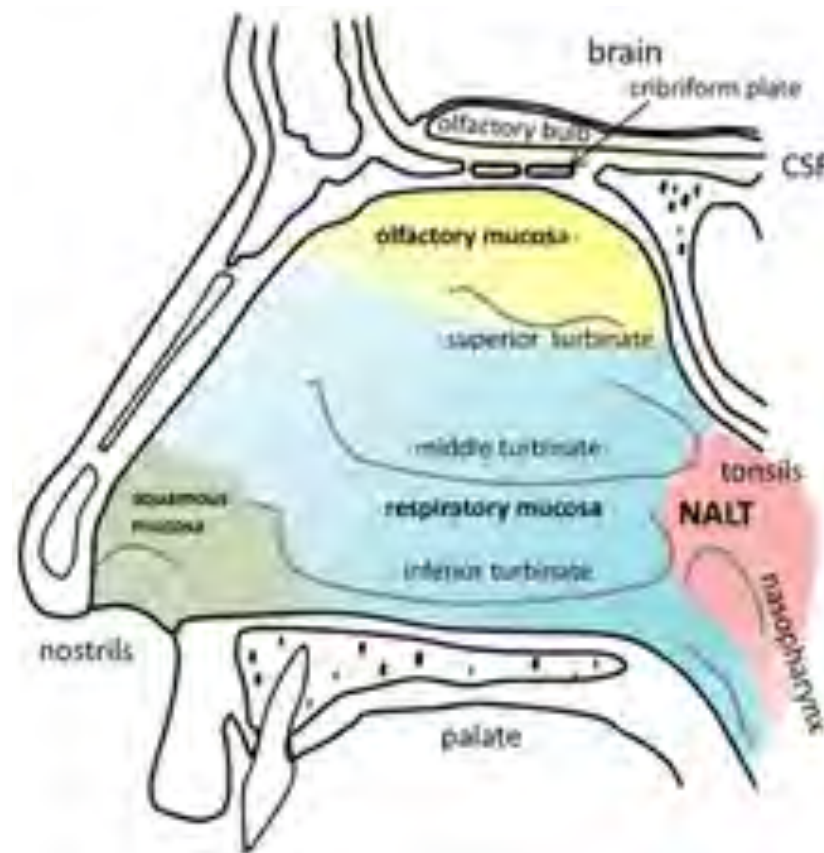
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Use of a Sectional Adult Nasal Airway Model for the Evaluation of Nasal Delivery Devices and Administration Techniques

BACKGROUND

- The human nasal cavity is a target for both locally and systemically acting medications.
- However, it is difficult to evaluate drug deposition with different nasal devices and administration techniques in the complex nasal passageways, and in particular at the olfactory region, where there is the potential to bypass the blood-brain barrier.



The nasal cavity.
(Wikipedia)

Nasal Model Development

- Two variants of a sectional adult nasal airway model were developed based on data from an adult MRI nasal scan.
- The study purpose was to visualize deposition patterns and measure regional deposition from a new nasal nebulizer (NasoNeb*, Nasoneb Inc., Plattsburgh, NY).
- The models were derived from a MRI scan of a 53-year old male subject, reported by Guilmette RA and Gagliano TJ¹.
- The original model geometry has been used multiple times in particle deposition simulations and experiments for the Lovelace Research Institute of Albuquerque, NM.



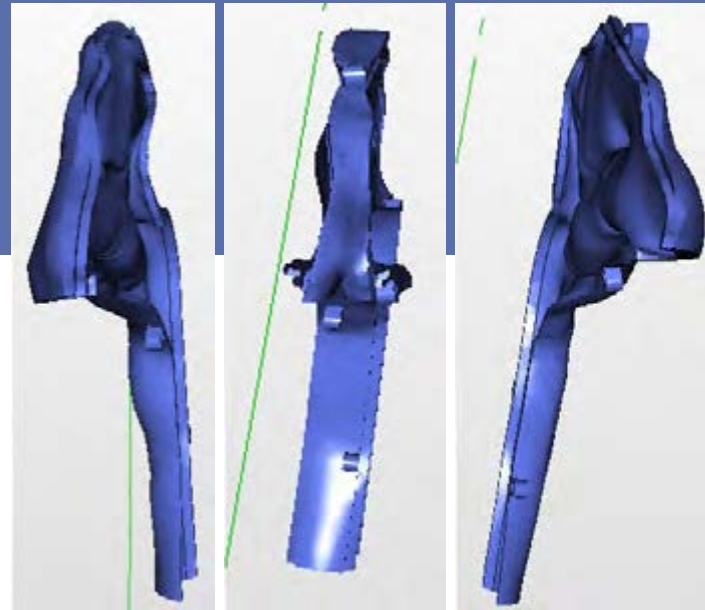
NasoNeb* Sinus Therapy System
with handheld cup

¹ Guilmette RA and Gagliano TJ. Construction of a model of human nasal airways using in vivo morphometric data. Ann. Occ.Hyg. 1994;38(Suppl. 1):69-75.

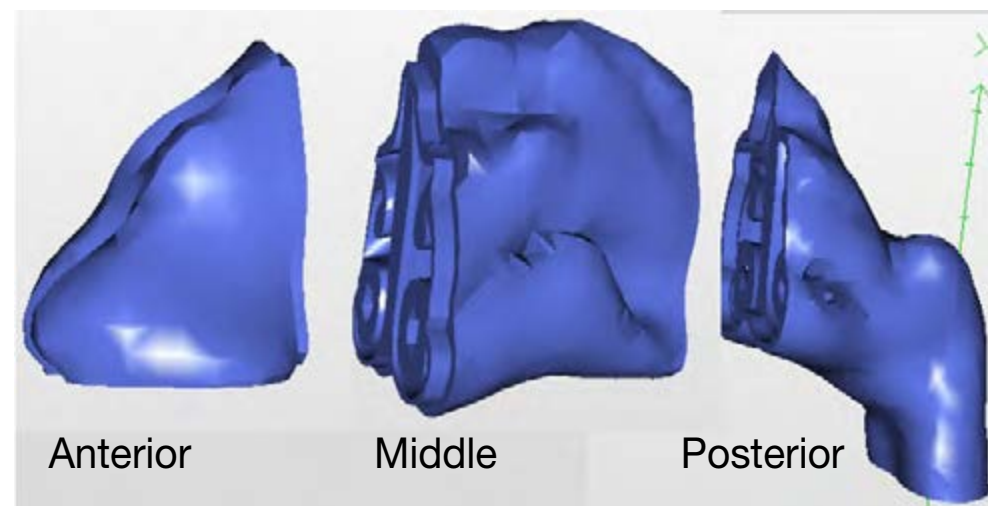
METHODS

Model 1

- Model 1 was longitudinally segmented and transparent to permit deposition to be visualized directly



CAD images for Model 1



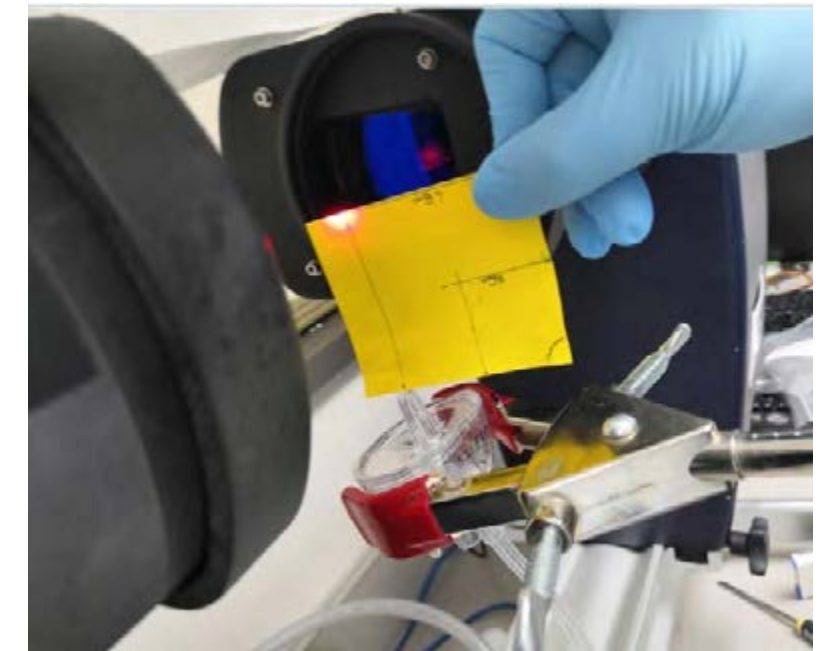
CAD images for Model 2

Model 2

- The second model was segmented horizontally into anterior, middle and posterior passageways
- It was made from sintered nylon (opaque) to be chemically compatible with API recovery solvents

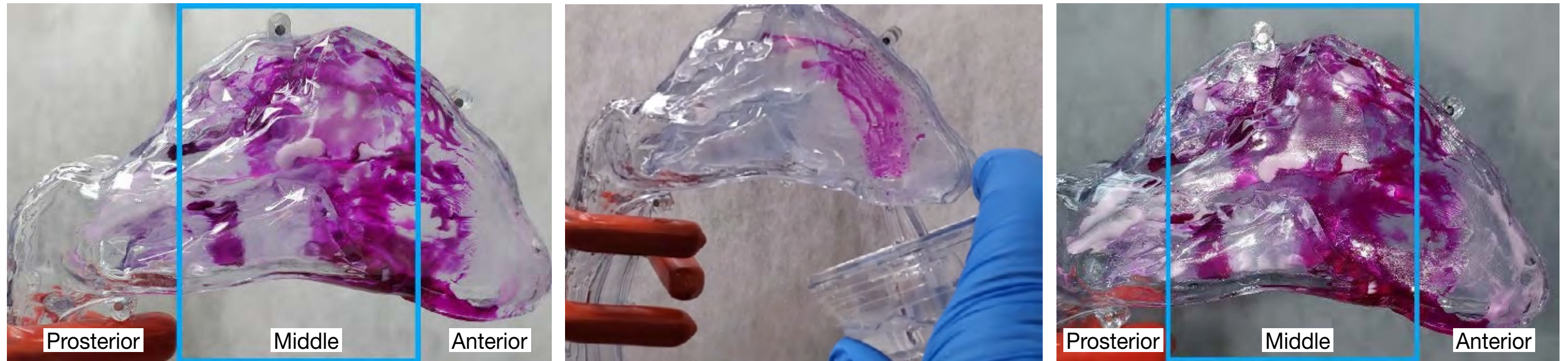
Quantitative Observations — Laser Diffractometry

- Droplet size distribution measurements were made by Spraytec Laser Diffractometry (LD) ($n = 3$ replicates at 6 cm working distance), spraying the droplets from the Nasoneb* nasal nebulizer directly into the optical pathway
- These measurements were made to quantify the water droplet size distribution accompanying the suspended budesonide particles



Spraytec LD with Nasoneb* nasal nebulizer located beneath the optical pathway

RESULTS

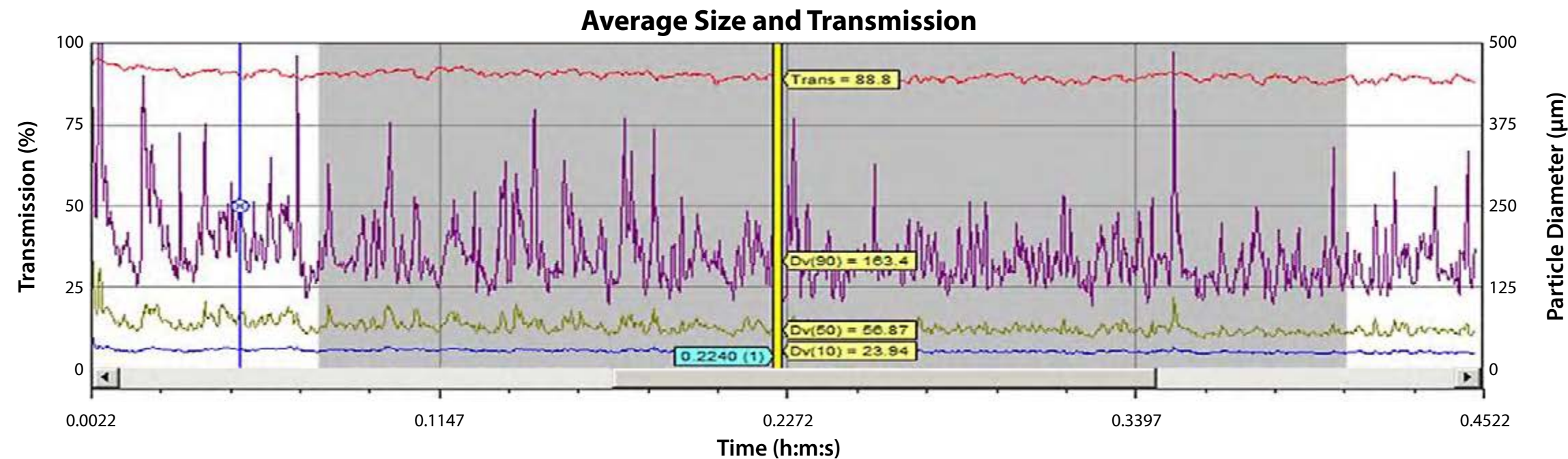


Representative images following delivery of a spray containing budesonide (500 µg/2 mL) delivered from a Pulmicort[†] Nebuamp[†] via the Nasoneb^{*} nasal nebulizer

Visual Observations With Model 1

- A colour-presenting water-finding product (Sar-Gel[†], Sartomer Americas, Exton, PA) was used to visualize budesonide deposition based on the accompanying water in the formulation
- Most of the deposition occurred in the middle segment

LD-Derived Measurements

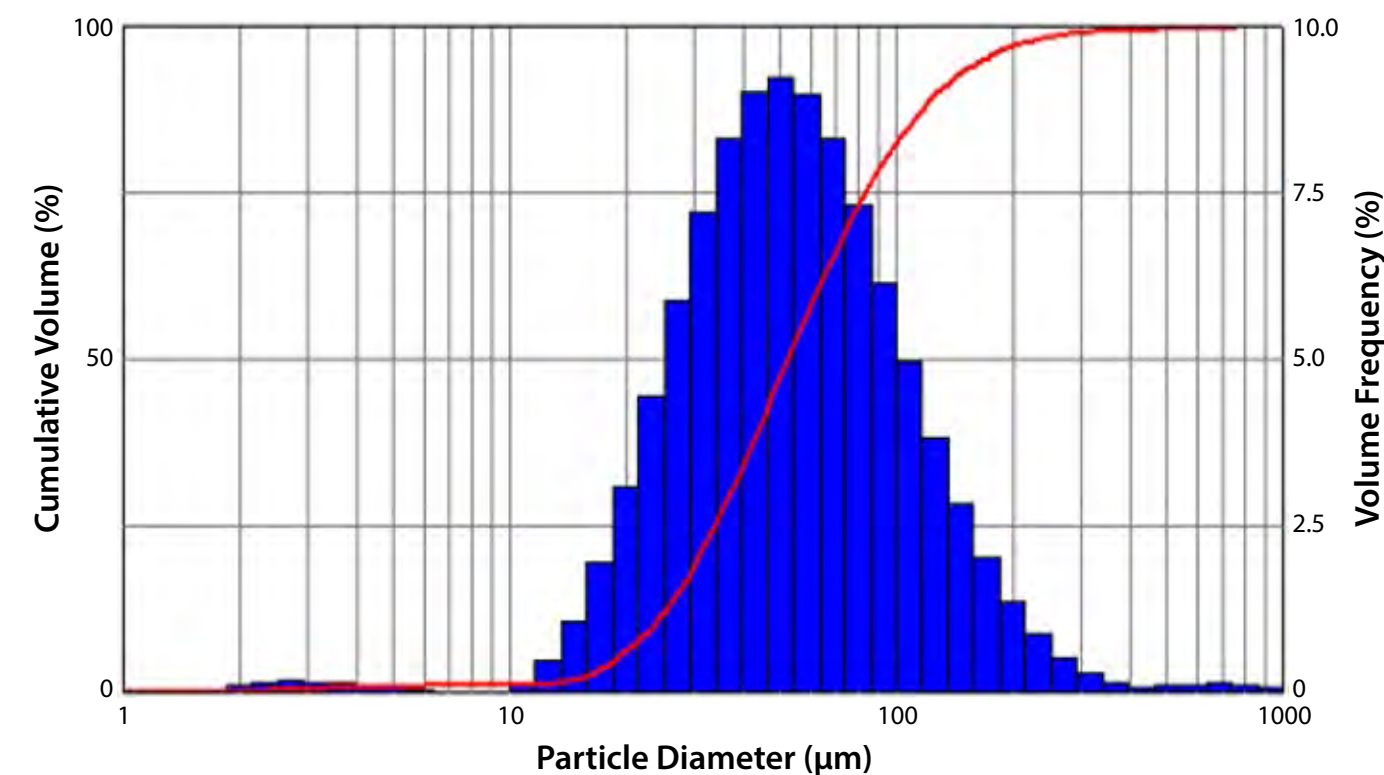


Representative images following delivery of a spray containing budesonide ($500\text{ }\mu\text{g}/2\text{ mL}$) delivered from a Pulmicort* Nebuamp* via the Nasoneb* nasal nebulizer

- The LD provided measures of 10th, 50th (median) and 90th volume percentiles of the distribution
- The Volume Median Diameter (VMD) corresponding to the 50th percentile was chosen as being most representative measure of where the bulk of the accompanying budesonide would deposit in Model 2

LD-Derived Measurements

Size-resolved histogram of water droplets from Nasoneb* nasal nebulizer



- The Dv_{50} (VMD) values were consistent with the observed water droplet deposition profile in Model 1 in which most colour was evident in the middle segment

Spraytec LD Droplet Size Measurements (μm)

Dv_{10}	Dv_{50}	Dv_{90}
21.0 ± 1.1	56.1 ± 4.0	231.5 ± 3.9

Deposition Of Budesonide Particles In Model 2

Budesonide Recovery by Region in Model 2

(mean $\pm$ SD, $n = 3$ replicates)

Anterior	Middle	Posterior
81 $\pm$ 16 μ g	173 $\pm$ 58 μg	39 $\pm$ 29
28 $\pm$ 4 %	58 $\pm$ 13 %	15 $\pm$ 12 %

- The bulk of the budesonide was recovered from the middle segment of the model
- This outcome is consistent with the results from the visual observations with Model 1 and separate LD measurements

CONCLUSIONS

- The LD-based water droplet size distribution data together with the budesonide recovery from Model 2 helped confirm the visual observations with the transparent Model 1 that showed the bulk of the deposition occurred in the middle/turbinate region of the nose model
- These adult models are likely suitable for further investigations into regional deposition of inhaled sprays via the nasal route