What is being treated where?

- Affects preferred route of delivery

- Inhaled drug delivery
  - Expensive to develop
  - Device adds to prescription cost
  - Multiple inhalers not popular with patients
  - Cannot be used with coloured drugs or those with unpleasant taste or effects on taste perception
    - Can also change saliva colour
  - Not constrained by Lipinski rules

- Oral drug delivery
  - Constrained by Lipinski rules
    - 'Rule of 5' (limits type of molecule you can design)
  - Greater off-target vulnerabilities
  - Compounds need to have ultraclean toxicology

Inhaled Therapy

- To non-experts an easy, fast, cheap option

- In reality inhaled therapy is difficult
  - Oral DMPK hurdles become challenges to ensure efficacy, have acceptable physical form, potency and solubility etc.
  - However, Lipinski rules can sometimes be ignored
  - So, high PPB, FFP and poor bioavailability may be virtuous!
  - Potency must be high because device needs to contain many doses
  - For once daily dosing drug, and/or their effects must persist. This may be challenging for stability and selectivity reasons

Pharmaceutical profiling

- Inhaled drug development has uncommon requirements
  - Pharmaceutical profile of compounds is an important decision tool in discovery
  - Profiling mitigates later risks
    - Insures against unpredictable slower developability
  - Profiling gives physical properties early emphasis
    - Crystallinity, solubility, low hygroscopicity
    - Thermal behaviour (Thermal stability)
    - Particle behaviour
    - Stability with likely excipients

Compounds lacking appropriate physical properties are not developable assets for inhalation from DPI devices