in vitro inhalation model
**Why? In vitro test for inhalation exposure route**

Inhalation is important route for exposure:
- intentional: drug delivery (pharmacy)
- non-intentional: risk's of chemicals (workplace, consumer products etc.)

- In vivo animal models are not (always) a good representative to predict human situation
>40 year experience in inhalation studies

- Acute studies (single 4 hour exposure)
- Sub-acute studies (14-28 days)
- Sub-chronic studies (90 days)
- Chronic studies / carcinogenicity (1-2 years)
- Irritation (sensory) / Alarie test
- Respiratory allergy
- Combination with repro-studies, neuro-studies or genotox studies
- In vitro toxicity
- CxT (Concentration - time relationship in acute toxicity)
State of the art generation and monitoring techniques for vapours, gasses and aerosols

Custom-made designs

Aerosols containing:
- micro sized particles
- nano structured particles
- nano particles

Providing well controlled test atmospheres with challenging test substances

Materials tested:
- Chemicals (powders, liquids, vapours)
- Agro-chemicals (pesticides)
- Pharmaceuticals
- Food ingredients (enzymes)
In vitro human inhalation model

Combination of:
1. Representative primary human epithelial lung cells at a Air-Liquid Interface (ALI):
   - Nasal, tracheal or bronchial
   - Relevant morphology

2. Air exposure via module:
   - Testing of complex mixtures (gasses and particles)
Advantages of in vitro human inhalation model

- Relevant morphology (human origin)
  - Mucus production
  - Metabolism/ detoxification
  - Presence of tight junctions
  - Presence of ciliated cells/ ciliary beating

- Effect parameters:
  - Barrier function
  - Oxidative stress
  - Release of inflammatory mediators
  - Functional changes (ciliary beating, mucus production)
  - Cytotoxicity
  - Genotoxicity

- Potential reduction of animal use
Further development

- Assessment of various end points in the same model
- Combined efficacy, toxicity, PK

- Dynamic air exposure (Vitrocell)

- Validation/comparison with in vivo models and other in vitro models; ideally extrapolation to clinic/human studies
Would an *in vitro* test for the inhalation route be beneficial for you?

When would this in vitro test be of value for your company?

- Screening purposes, faster
- Less material needed
- Human relevancy
- Combined efficacy/toxicity (local effects)
- Complementary to in vivo experiments
- Replacement of in vivo experiments
- Other…
Why TNO?

› **Multidisciplinarity**
  - In vitro tox, in vivo tox, systems tox, risk assessment, PK modelling and analytical equipment/expertise all under the same roof

› **Innovative toxicity tests**
  - **Track record** in development and implementation of innovative *in vitro* (toxicity & PK) assays
  - **Excellent** in inhalation (in vitro/in vivo) and skin expertise
  - Extensive (chemicals/food/pharma) industry / SME / In vitro society / authorities **network** to efficiently embed innovations
  - Option for **partnering** with governmental matching (ELIco)
  - **Quality** Standard
Contact information:

Ingeborg Kooter
Ingeborg.kooter@tno.nl
+31-6-10670491