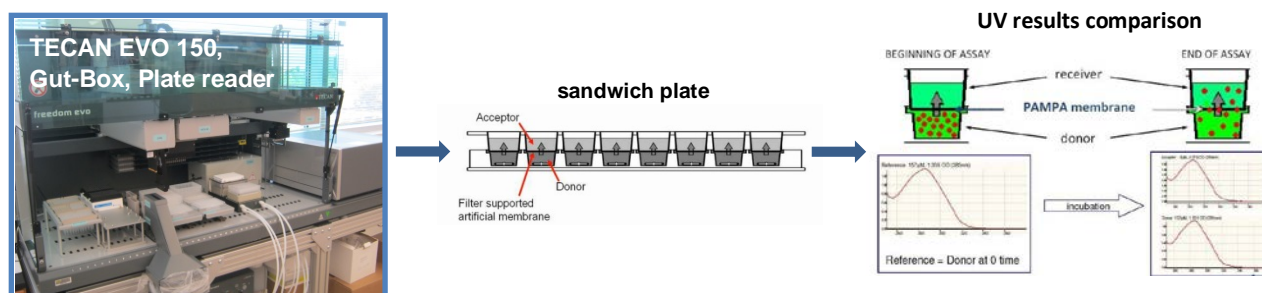


CPAS Focus on Technology: High throughput Parallel Artificial Membrane Permeability Assay (PAMPA)

Instrument: TECAN EVO 150 automated workstation, TECAN infinite 1000 pro microplate reader

Screening Tools from Pion: Double-Sink™ PAMPA, Gut-Box™ and PAMPA Evolution software

PAMPA is applied as an *in vitro* model of passive transcellular permeability. The Double-Sink PAMPA method uses an optimized mixture of phospholipids infused into lipophilic filter support which creates an artificial membrane. Such membranes immobilized on a filter are placed between a donor and acceptor compartments mimicking the cell barriers characteristic of gastrointestinal tract (GIT), the blood-brain barrier (BBB) and the skin. The GIT PAMPA will evaluate how the drug candidate might be absorbed across the gastrointestinal tract, the BBB PAMPA will predict the ability to a central nervous system (CNS)-targeting drug candidate for crossing the blood-brain barrier to reach its therapeutic receptors inside the brain, and the Skin PAMPA for pure API in solution, liquid semi-solid and patch formulation.



Each drug candidate is introduced to the donor compartment. After 30-60' minutes incubation/ stirring period using the Gut-Box, the concentration of drug in the donor and acceptor compartments is measured using UV spectroscopy.

- PAMPA proposes a fast and economical permeability screening of multiple drug candidates compared to cell based Caco2- or MDCK based screens, which need costly provision for cells.
- PAMPA implemented on the Tecan Freedom EVO 150 workstation (3 arms: 96 channels, 8-span liquid handler and robotic manipulator; plate reader: Infinite 1000 pro microplate reader) with fully automated data collection is capable of analyzing up to 600 samples per day.

Selected References and Information

- (1) Avdeef, A. *et al.* "Caco-2 permeability of weakly basic drugs predicted with the Double-Sink PAMPA pKflux method." *Pharm. Sci.*, **2005**, *24*, 333-349.
- (2) Tsinman O. *et al.* "Physicochemical selectivity of the BBB microenvironment governing passive diffusion – matching with a porcine brain lipid extract artificial membrane permeability model." *Pharm. Res.* **2011**, *28*, 337-363.
- (3) Sinko B. *et al.* "Skin-PAMPA: a new method for fast prediction of skin penetration." *Eur J Pharm Sci.* **2012**, *45*, 698-707.

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