# TRANSIL$^{XL}$
# Intestinal Absorption Kit

## A Fast High-Throughput Assay for Predicting Intestinal Permeability & the Volume of Distribution

### FEATURES AND BENEFITS

- Fast, requires only 20 minutes total assay time
- Measures the affinity to phosphatidylcholine membranes and predicts intestinal permeability and the volume of distribution
- Ready-to-use format in 96-well plate format generating highly reproducible results
- Rapid compound quantification due to immoblized brain membranes
- Kit includes a spreadsheet for calculation of final results and traffic light system for data quality rating

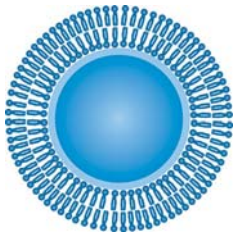

Fig. 1: Illustration of a TRANSIL Intestinal Absorption bead with a single lipid bilayer reconstituted from egg yolk phosphatidylcholine.

### TECHNICAL DESCRIPTION

The TRANSIL$^{XL}$ Intestinal Absorption kit measures the affinity of drugs to phosphatidylcholine membranes. It is not only a screening tool to predict intestinal permeability coefficients, but also to predict compounds' tissue binding. As drug-membrane interactions are key to both the process of membrane permeability and to binding to and permeating into the cell membranes of tissues the assay kit is an ideal tool to predict intestinal permeabiliity rates as well as the volume of distribution already early in drug discovery.

The kit consists of ready-to-use 96 well microtiter plates. One plate can be used for predicting intestinal permabilty and volume of distribution of up to 12 compounds. The assay requires only 5 steps: (i) addition of drug candidate, (ii) mixing and incubation for 12 minutes, (iii) removal of beads by centrifugation, (iv) sampling of supernatant, and (v) quantification of drug candidate.

### CAPABILITIES

- Detection systems
  - LC/MS/MS
  - Scintillation counting
  - Others
- Parameters estimated and predicted
  - Intestinal permeability rates
  - Volume of distriubtion (VD)

**Sovicell**
Deutscher Platz 5b 04103 Leipzig t. +49 341 520 44 0 f. +49 341 520 44 12 e. info@sovicell.com www.sovicell.com

## Application and Relevance

The ability to prospectively predict the pharmacokinetics of new chemical entities in humans is a powerful means by which scientists involved in the discovery of new drugs can select for further development only those compounds with the potential to be successful therapeutic agents. Absorption of an orally administered drug from the GI tract is a complex process that is influenced by various factors. The permeability and/or solubility can limit the fraction dose absorbed of a drug. During the lead optimization process, identifying the causes of poor bioavailability is very important, because it can help to guide the synthesis program toward candidates with a more suitable pharmacokinetic profile and, thus, a higher chance for successful development.

The volumue of distribution (VD) represents a complex combination of multiple chemical and biochemical phenomena. It is a measure of the relative partitioning of a drug between plasma (the central compartment) and the tissues. Thus, the VD term considers all of the tissues as a single homogeneous compartment. VD has a strong influence on a drugs half-life and thus affects the dosing regimen. Drugs with short half-lives are likely to be administered more frequently than those with long half-lives. Early prediction of the volume of distribution is therefore an instrumental parameter for compound selection.

## Validation

Literature reported values for intestinal permeability (caco-2) and volume of distribution were collected for 43 compounds and compared with predictions of $P_{int}$ (fig. 2) and VD (fig. 3) generated by the spreadsheet supplied with the TRANSIL$^{XL}$ Intestinal Absorption kit. The predictions of $P_{int}$ are based on a hybrid model incorporating the membrane affinity measurement and chemical descriptors of the compounds, while the VD predictions are based on the membrane affinity and plasma protein binding measurements. Both models yield good predictions for early discovery and lead optimization.

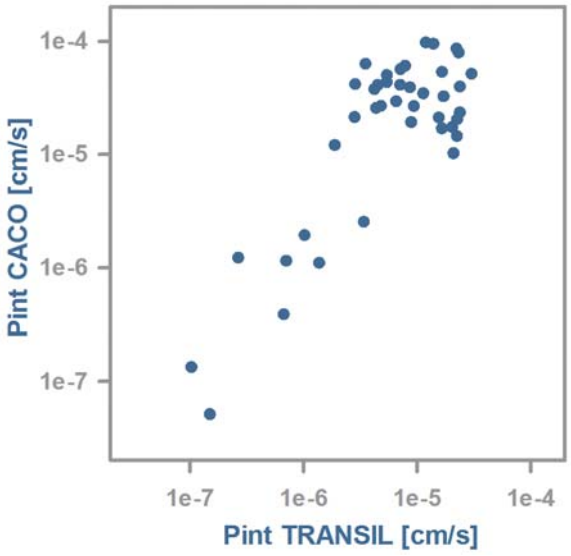


Fig. 2: Correlation of the TRANSIL predicted intestinal permeability rate and the passive component of permeabilities measured in caco-2 eperiments indicating that the predictions based on membrane affinity and chemical structure yield acceptable early predictions of passive permeabilty ($r^2$=0.7).

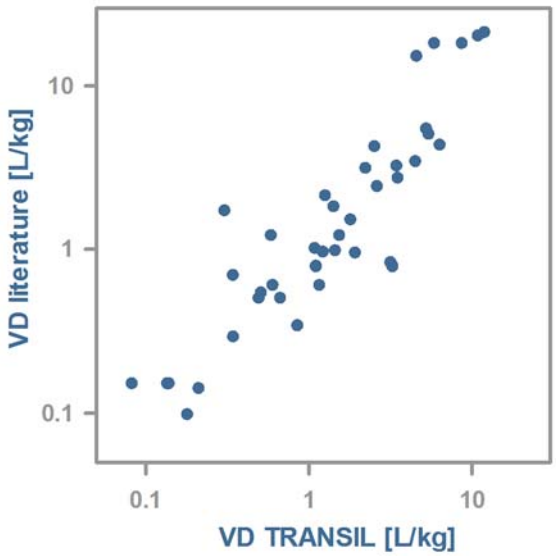


Fig. 3: Correlation of the TRANSIL predicted volume of distribution (VD) and literature reported volumes of distribution for a set of 43 marked drugs. The VD predictions of the TRANSIL$^{XL}$ intestional absorption kit yield an $r^2$ ogreater than 0.8 and thus meet expectations of early drug discovery.

## PRODUCT INFORMATION

| Order Number | Name |
|---|---|
| TMP-0100-2096 | TRANSIL$^{XL}$ Intestinal Absorption kit |

V008.12.08.27

**Sovicell**
Deutscher Platz 5b 04103 Leipzig t. +49 341 520 44 0 f. +49 341 520 44 12 e. info@sovicell.com www.sovicell.com