The Final EUTOXRISK Symposium 16

Prediction of developmental and reproductive toxicity (DART): a read-across case study with short branched carboxylic acids

Dinant Kroese, Andre Wolterbeek (TNO), Tanja Waldmann, Jaffar Kisitu, Jonathan Blum, Marcel Leist (UKN), Claudia McGinnis, Manuela Jaskin, Stefan Kustermann (ROCHE), Katharina Brotzmann, Thomas Braunbeck (UHEI), Bjorn Koch (LUMC), Barbara van Vugt, Bart van der Burg (BDS), Ciaran Fischer, Iain Gardner, Oliver Hatley, Richard MacClenon (Cyprotex/CERTARA), Ségolène Siméon, Frederic Bois (INERIS/CERTARA), Tony Long (LHASA), Ulf Norinder (KI), Barbara Drzazil (UNIVIE)

Coordinated by: TNO

Regulatory context: REACH

Case Study Testing Approach

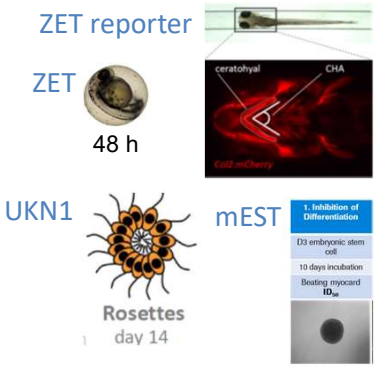
Applying the following NAMs to MHA and several structural similars having DART data:

- *In vitro* DART battery (toxicodynamics)
- *In silico/in vitro* TK & PBTK (toxicokinetics)
- Data integration statistical models

Case Study Toxicodynamics NAM Toolbox

Applied *in vitro* DART battery:

- Zebrafish embryo test (ZET)
- ZET CHA reporter (cranio-facial differentiation) (ZET Reporter)
- Human neural stem cell differentiation model (UKN1)
- Mouse embryonic stem cell differentiation model (mEST)
- CALUX reporter assay panel (CALUX; n=20)

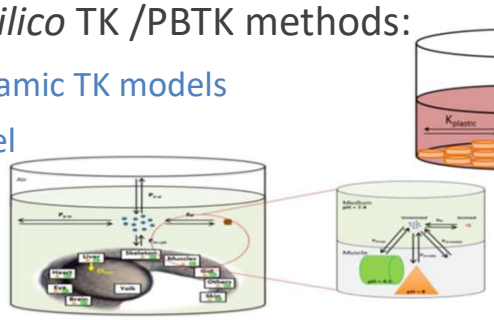


To derive in vitro toxicological profile and nominal point of departure (PoD) for each chemical

Case Study Toxicokinetics NAM Toolbox

Applied *in silico* TK /PBTK methods:

- Static & dynamic TK models
- ZET TK model



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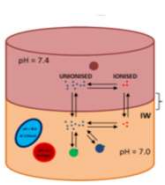
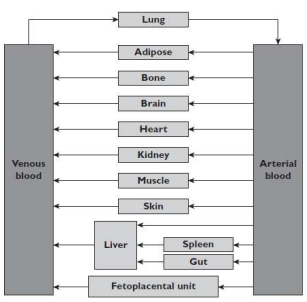
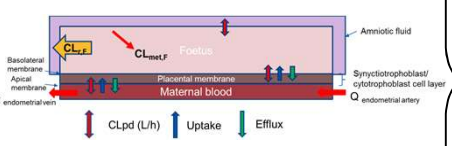


Convert nominal PoD to 'free' PoD

- PBTK model (incl. placenta)





Convert 'free' PoD to oral equivalent dose for risk assessment

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