

TOXVIT - GVK BIO
In Vitro Toxicology Solutions



Modern Toxicity Testing Technology



More Robust Mechanistic Data



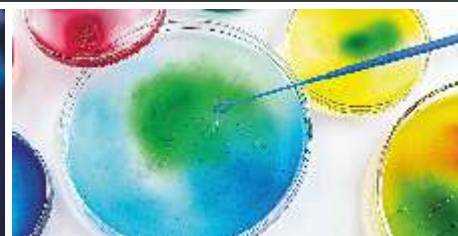
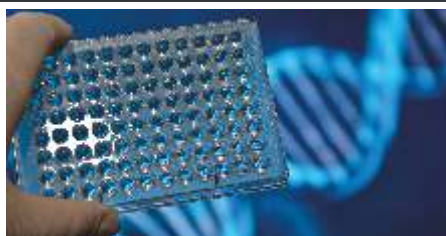
Reduce Cost and Testing Time



Decisions on Human Relevant Dose Levels



Validated Quick Clear Testing Protocols



Platforms used for Toxicity Testing

- High Content Imaging - Thermo Scientific Cell Insight CX7 Platform
- Multimode Reader - Perkin Elmer Envision 2104 Platform
- Flow Cytometry - BD FACS Verse Platform
- Agilent Platform for HPLC
- RT PCR - Applied Biosystems QuantStudio 6 Flex Platform
- Next Gen Sequencing - Illumina Platform

Technologies used for Toxicity Testing

- Primary Cell Culture Technology
- PSC - Pluripotent Stem Cell Technology
- 3D Microtissue Culture Technology

In Vitro Toxicity Testing



Multi-parametric Cytotoxicity

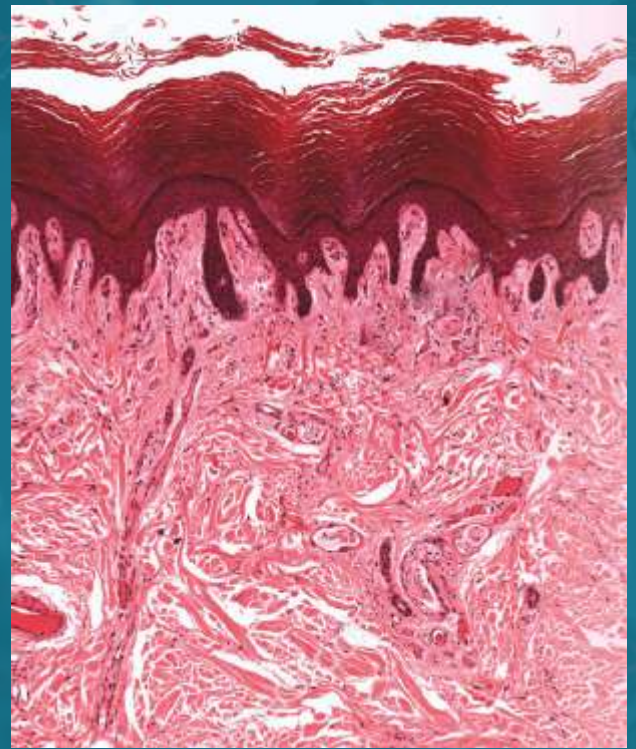
- IC50 determination
- Cell loss/death (fluorescent imaging)
- Nuclear size and morphology (fluorescent imaging)
- Cell membrane permeability (fluorescent imaging)

Note: About 50 different cell lines of human origin are available for cytotoxicity testing



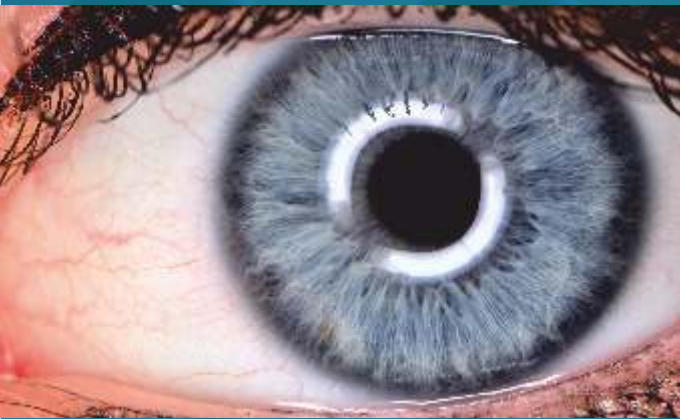
Genetic Toxicity Testing

- Bacterial Reverse Mutation Test (Ames Test)- Plate Incorporation methods (OECD 471)
- Ames Test 6 well and 24 well plate method (Plate incorporation method).
- Bacterial Reverse Mutation Test - Uses Xenometrix AG - ANIARA microplate kit method (OECD 471)
- *In Vitro Mammalian Cell Micronucleus Test* - Using CHO, CHL, A549 cell lines & Human PBMCs including cytotoxicity assessment on HCS platform (OECD487)
- *In Vitro Mammalian Chromosomal Aberration Test* - Using CHO cell line & Human PBMCs including cytotoxicity assessment (OECD 473)
- *In Vitro Mammalian Cell Gene Mutation Tests* - MLA (L5178YTK+/- cell line) & HPRT (CHO-K1 cell line) mutations (OECD 490/476)
- *In Vitro Comet Assay* - Using PBMC, CHO, CHL test systems on HCS platform
- H2AX Double Strand DNA Damage Response Assay - Using A549, HepG2 & BEAS-2B cell lines on HCS platform
- ToxTracker Assay.



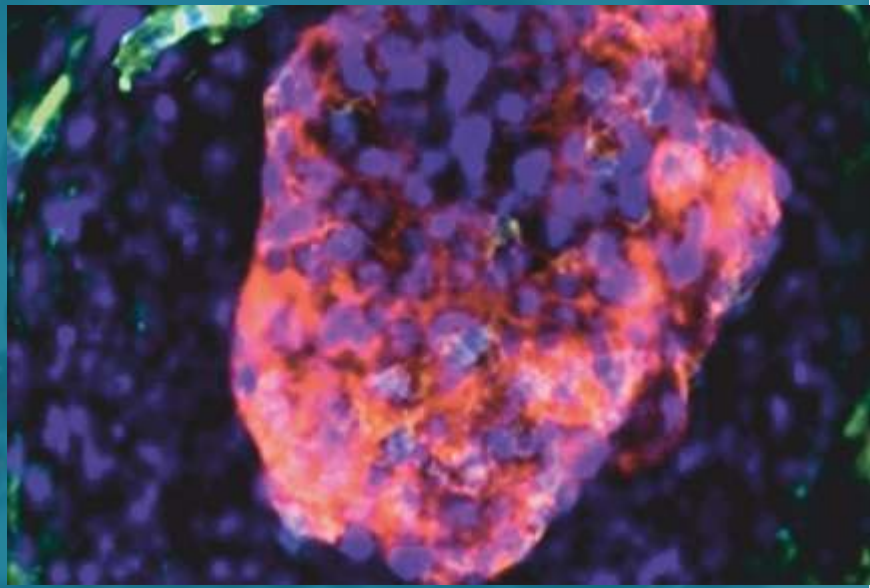
Dermal Toxicity

- *In Vitro Skin Irritation* - Using 3D reconstructed human epidermis models (OECD 439)
- *In Vitro Skin Sensitisation* - Using 3D reconstructed human epidermis models (OECD 431)
- Phototoxicity Assay - Using Balb/C 3T3 cells
- *In Vitro Skin Sensitisation* - Using KeratinoSens cell line (OECD 442D)
- In Chemico Skin Sensitisation - Direct peptide reactivity assay (OECD 442C)



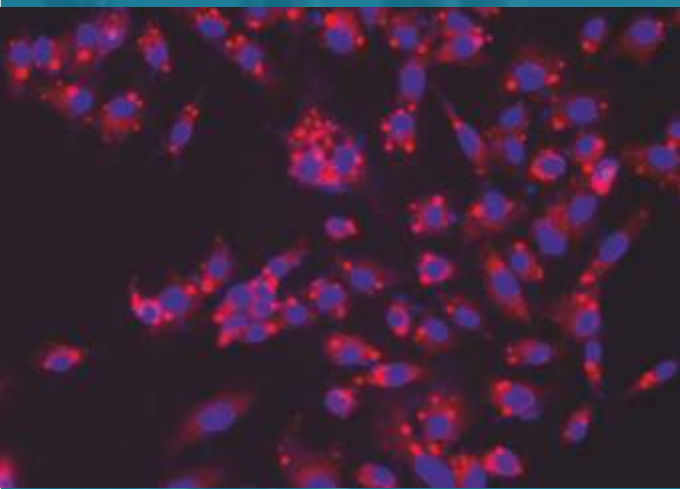
Ocular Toxicity

- Short Time Exposure *In Vitro* Test Method for Identifying – Using corneal epithelial cells (Statens Seruminstitut Rabbit Cornea SIRC) cell line (OECD 491)
- Reconstructed Human Cornea-like Epithelium (RhCE) Test - Using 3D reconstructed human corneal epithelium (HCE) tissue model (OECD 492)



Cardiotoxicity

- hERG Safety Screening – Using Invitrogen's Predictor™ hERG fluorescence polarization assay kit
- 3D Microtissue based Cardiotoxicity Assay - Using Human iPSC - CM (cardiomyocytes) spheroid Cultures



Hepatotoxicity

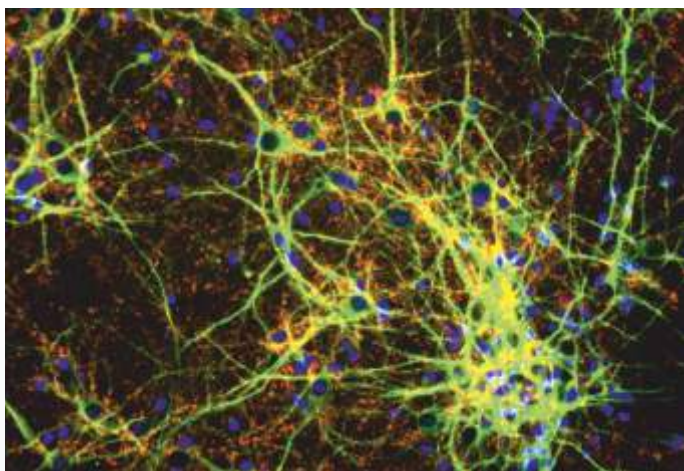
Hepatotoxicity panel - Using HepG2, HUH7, Hep3B cell lines & Human iPSC HepRG spheroid cultures

- Drug induced phospholipidosis & steatosis
- Lysosomal trapping (lysosomotropism)
- Cholestasis
- Mitochondrial permeability transition



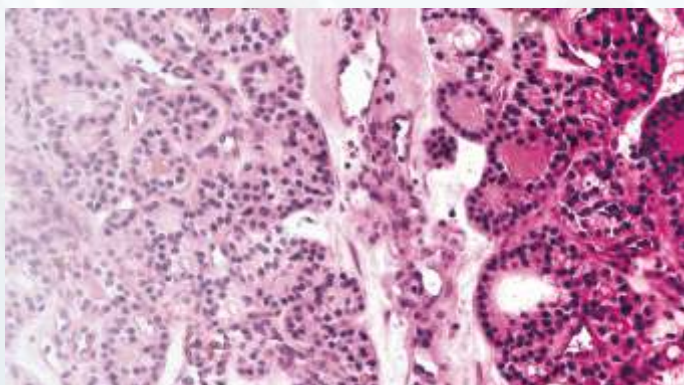
Mitochondrial Toxicity

- Mitochondrial (Glu/Gal) Assay - In glucose & galactose supplemented media
- Mitochondrial membrane potential & cytochrome release



Neurotoxicity

- Developmental Neurotoxicity
- NeuriteOut growth Assay
- Synaptogenesis Assay



Endocrine Disruption Screening

Estrogen Receptor & Androgen Receptor Binding Assays -

- Using polar screen human full length ER (Alpha/Beta) competitor assay and polar green rat androgen receptor competitor assay fluorescence polarization assay kits
- Using ligand binding assays for ER and AR from rat membrane preparations (OPPTS/OCSP 890.1250 & OPPTS/OCSP 890.1150)
- Steroidogenesis Assay - Using H295R cell line with testosterone parameter assay kit and Estradiol parameter assay kit (R&D systems) (OECD 456)
- Aromatase Assay – (OPPTS/OCSP 890.1200)
- Androgen Receptor and Estrogen Receptor Reporter Assay

Toxicogenomic Profiling

- Toxicological Gene Regulation Studies – Relative and quantitative expression of metabolic and toxicological pathway regulatory biomarkers using RT-PCR and NGS platforms



Exploratory Toxicology

- Single dose 14-day acute toxicity study in rodents
- Repeat dose 28-day acute toxicity study in rodents

In Vitro Toxicology Solutions

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Leading Small Molecule CRDO



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