

# TOXVIT - Aragen *In Vitro* Toxicology Solutions



Modern Toxicity  
Testing Technology



More Robust  
Mechanistic Data



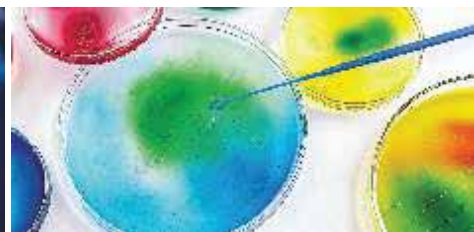
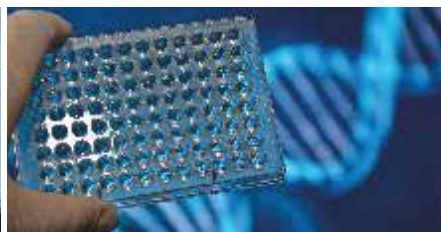
Reduce Cost  
and Testing Time



Decisions on Human  
Relevant Dose Levels



Validated Quick Clear  
Testing Protocols



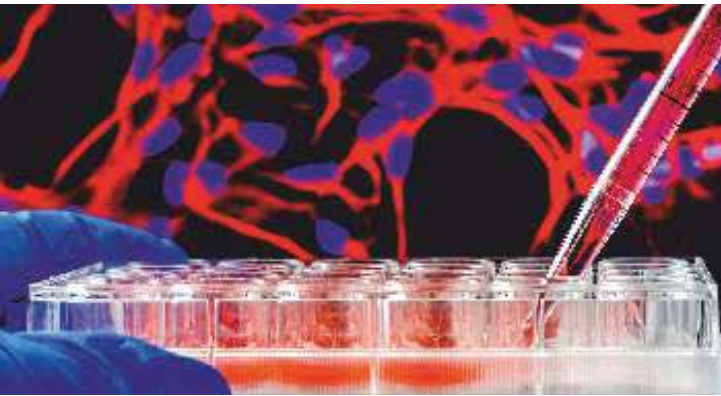
## Platforms used for Toxicity Testing

- High Content Imaging - Thermo Scientific Cell Insight CX7 Platform
- Multimode Reader - Perkin Elmer Envision 2104 Platform
- Flow Cytometry - BD FACS Verse Platform

## Technologies used for Toxicity Testing

- Primary Cell Culture Technology
- PSC - Pluripotent Stem Cell Technology
- 3D Micro Tissue Culture Technology

# In Vitro Toxicity Testing



## Multi-parametric Cytotoxicity

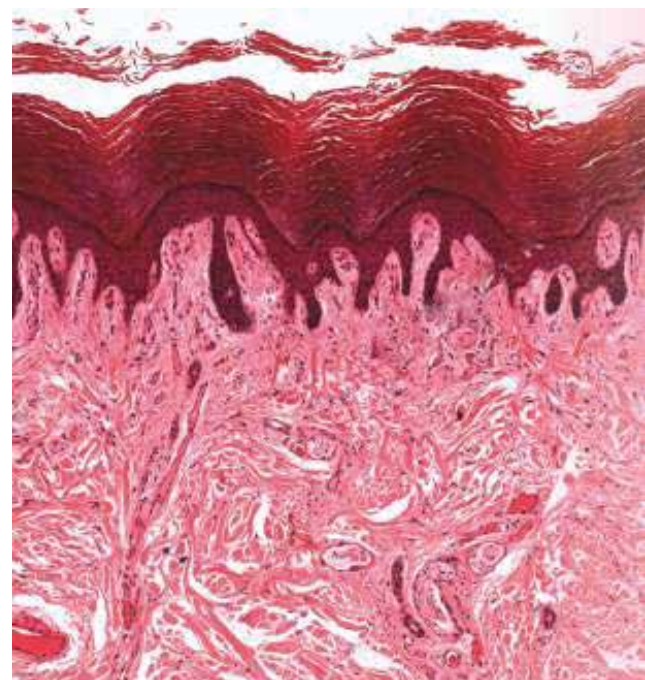
- IC50 determination
- Cell loss/death (fluorescent imaging)
- Nuclear size and morphology (fluorescent imaging)
- Cell membrane permeability (fluorescent imaging)

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



## Genetic Toxicity Testing

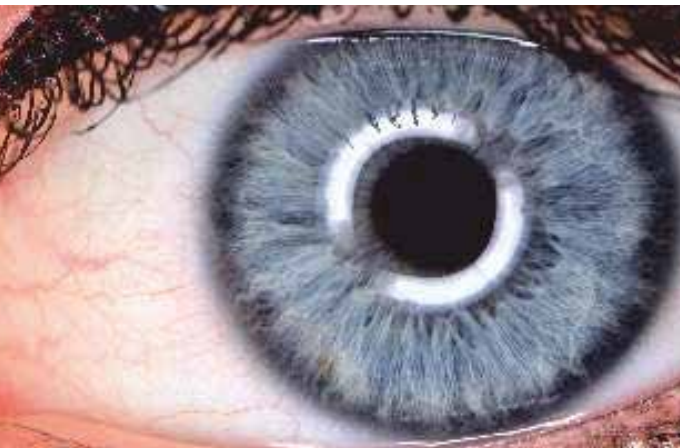
- Bacterial Reverse Mutation Test (Ames Test)- Plate Incorporation methods (OECD 471)
- Ames Test 6 well and 24 well plate method (Plate incorporation method).
- Bacterial Reverse Mutation Test - Uses Xenometrix AG - ANIARA microplate kit method (OECD 471)
- In vitro Mammalian Cell Micronucleus Test - 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

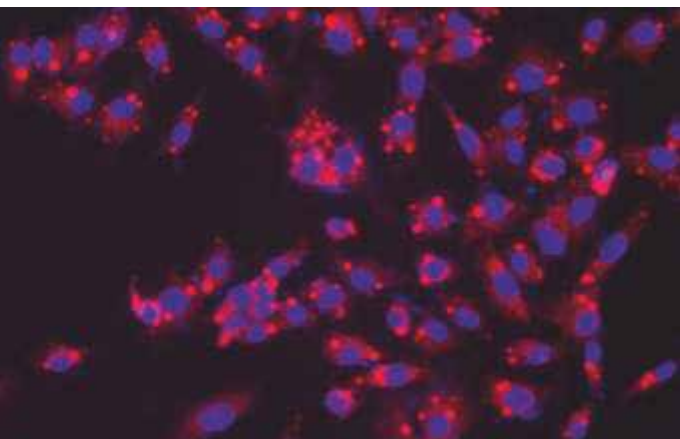
- *In vitro* Skin Irritation - Using 3D reconstructed human epidermis models (OECD 439)
- *In vitro* Skin Sensitisation - Using 3D reconstructed human epidermis models (OECD 431)
- Phototoxicity Assay - Using Balb/C 3T3 cells (OECD 432)
- *In vitro* Membrane Barrier Test Method for Skin Corrosion (OECD 435)
- *In vitro* Skin Sensitisation - Using KeratinoSens cell line (OECD 442D)
- *In vitro* Chemico Skin Sensitisation - Direct peptide reactivity assay (OECD 442C)





### Ocular Toxicity

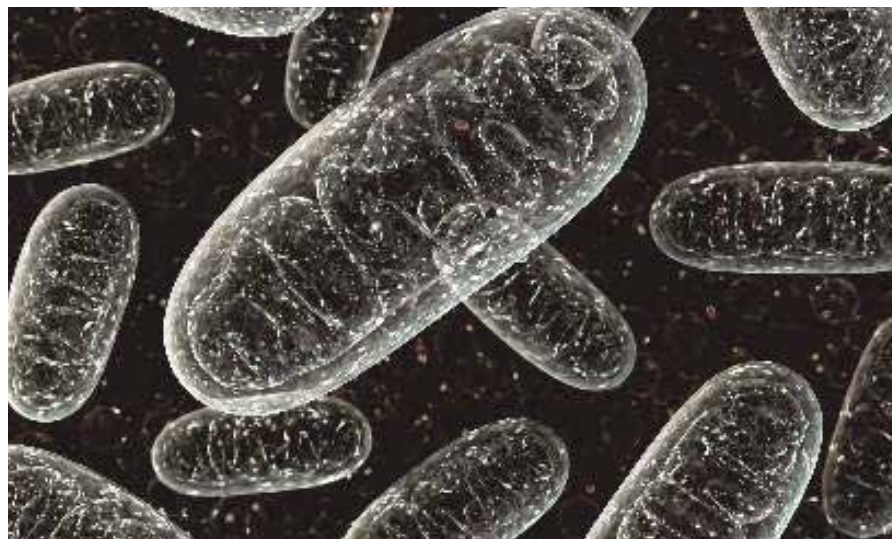
- Short Time Exposure **In vitro** Test Method for Identifying – Using corneal epithelial cells (Statens Seruminstitut Rabbit Cornea SIRC) cell line (OECD 491)
- Reconstructed Human Cornea-like Epithelium (RhCE) Test - Using 3D reconstructed human corneal epithelium (HCE) tissue model (OECD 492)
- Bovine Corneal Opacity and Permeability (BCOP, OECD 437)



### Hepatotoxicity

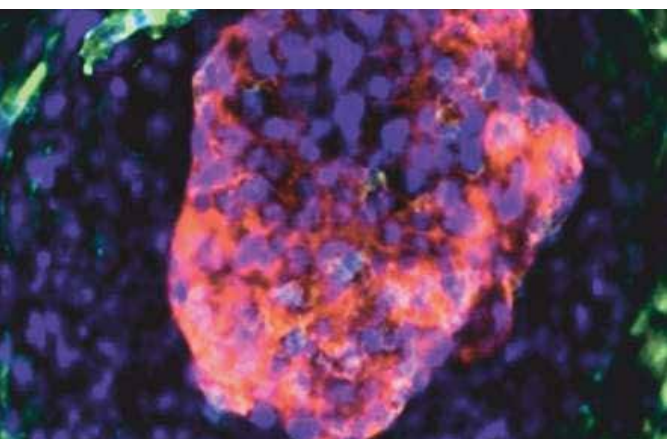
Hepatotoxicity panel - Using HepG2, HUH7, Hep3B cell lines & Human iPSC HepRG spheroid cultures

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



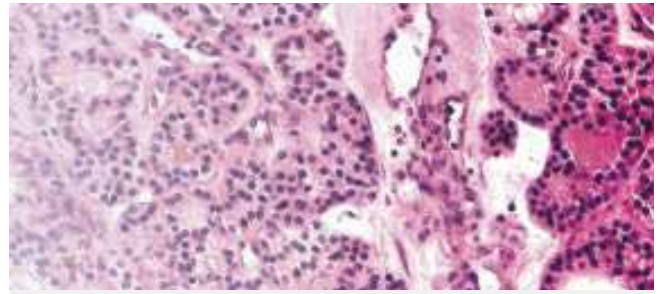
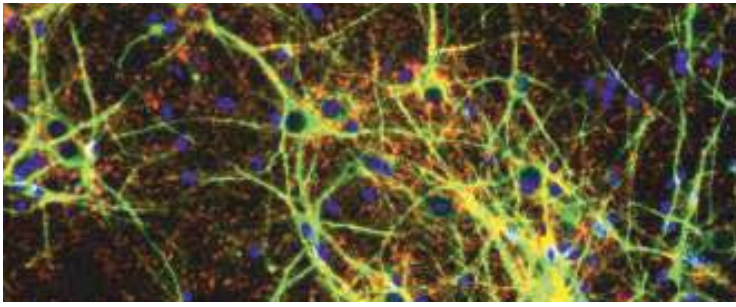
### Mitochondrial Toxicity

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



### Biomedical Device/Bio-reactivity assay (ISO 10993 or USP 87)

- MEM Cytotoxicity Test using L929 cell line
- Neutral red uptake (NRU) cytotoxicity test using Balb 3T3 Cell line
- MTT Cytotoxicity Test using L929 Cell line
- XTT cytotoxicity Test L929 Cell line



### Neurotoxicity

- Developmental Neurotoxicity
- Synaptogenesis Assay
- Neurotoxicity screening across a panel of Cell lines (HepG2, HuH7, Hep3B, SH-SY5Y, SK-N-SH)



### Genotoxicity tests for medical devices (ISO 10993-3):

- A test for gene mutation in bacteria (OECD 471)
- A test for gene mutation in Mammalian cells (OECD 476)
- A test for clastogenicity in mammalian (OECD 473)
- *In vitro* Mammalian Cell Gene Mutation Tests - MLA (L5178YTK+/- cell line) & HPRT (CHO-K1 cell line) mutations (OECD 490/476)

### *In vitro* Immunogenicity assay

- *In vitro* Immunogenicity assay using PBMC

### 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

Let's begin the  
Conversation

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