

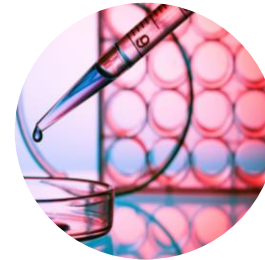


**PHARMA – FOOD HEALTH  
DERMATO COSMETIC - MEDICAL DEVICE  
CHEMICALS**

**ADME-Tox Specialists**

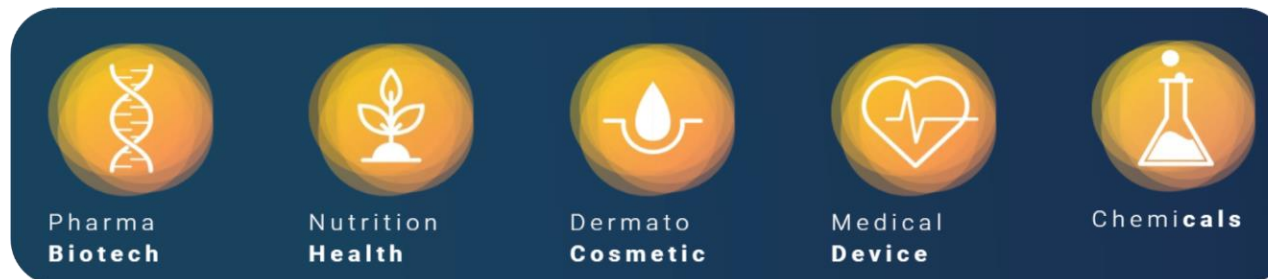
## ◆ Preclinical CRO Since 2004






- ◆ Biocitech Parc, Romainville, FR
- ◆ Cell cultures
- ◆ In-vitro studies
- ◆ Bio-analysis
  - ◆ Mass Spectrometry : LC-MS/MS – HR-MS
  - ◆ UV / Fluorescence / Luminescence
  - ◆ qPCR
  - ◆ Flux cytometry

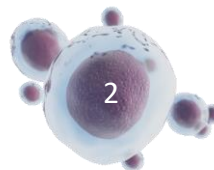


## ◆ GLP since 2011

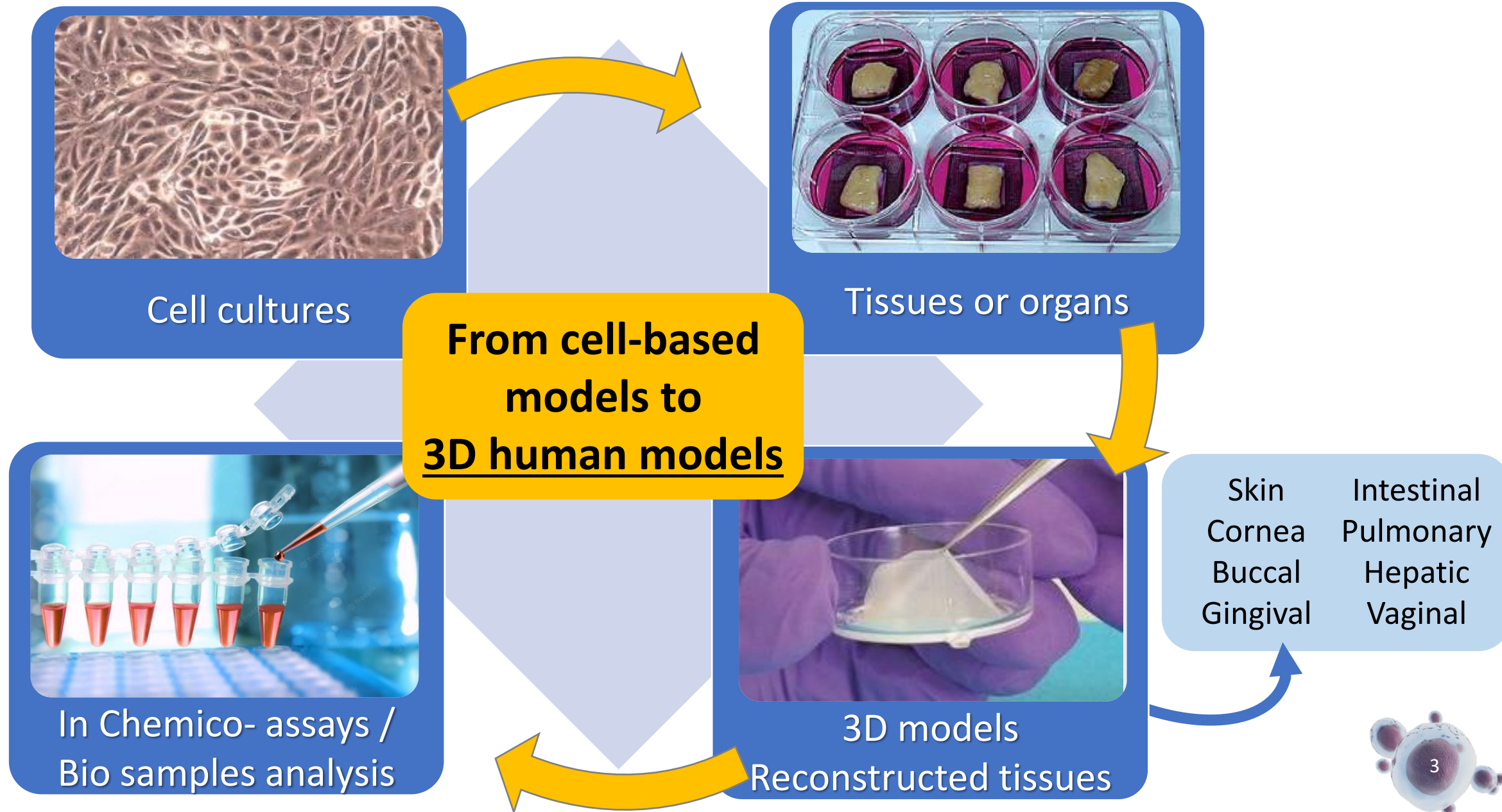
Expertise in 5 main industries



				
Pharma Biotech	Nutrition Health	Dermato Cosmetic	Medical Device	Chemicals



# Large portfolio of *in vitro* and *in chemico* tests



## Non-clinical safety studies

- Cosmetic
- Pharma
- Medical Devices



**GLP / ANSM  
Inspections**

- Chemicals



**GLP / COFRAC  
Inspections**



**ANSM**

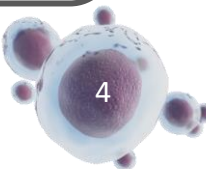
Pharma, Cosmetics,  
Medical Devices

**Cofrac**

Chemicals, Pesticides,  
Biocides

## Ready to use plated cells

**Producing and Marketing ready to use  
plated cells (INSERM License)**

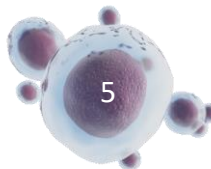




- ◆ > 100 Companies
- ◆ Since 2012
- ◆ Network of complementary activities
- ◆ Preclinical CROs
- ◆ Professionalism / reactivity / flexibility

- ◆ Assay distributorship agreement with Senzagen for GARD™ assay
- ◆ Broaden our respective batteries of assays and analyses to better address sensitization issues

- ◆ Public - Private platform
- ◆ Scientific pre-validation
- ◆ Novel in vitro methods
- ◆ Endocrine disruptors





◆ **R&D project management and technical support to develop alternative methods since 2005**

◆ **Proven track record in collaborative projects with major industrial actors and academics**

- Skin irritation ECVAM validation of RHE (L'Oréal, Coty) → Led to OECD TG 439
- Metabolism 3D models vs skin explants (L'Oréal) → Published by L'Oréal
- Irritation vs sensitization using 3D skin models (Unilever) → Published by Unilever
- Skin sensitization on RHE Model (Pierre Fabre Dermo-Cosmetic) → Publication released in 2016
- Skin genotoxicity on EpiSkin model (Galderma / Nestlé Skin health) → Publication released in 2018, presented to Cosmetic Europe
- DPRA MSMS / GLP → Eurotox2019
- Medium chain fatty acids as biomarkers for NASH (Galapagos) → Eurotox2019
- Equivalence of 3 commercially available forms of Vigabatrin, using 3 Human intestine models → GMP Lyon, October 2019
- Skin sensitization on EpiCs Model (Pierre Fabre Dermo-Cosmetic) → Published in 2020
- Skin photosensitisation Model (Pierre Fabre Dermo-Cosmetic) → Publication submitted
- Prevalidation of method for assessing potential Endocrine disruptors → PEPPER ongoing



ANSM

Pharma, Cosmetics,  
Medical Devices



Cofrac

Chemicals, Pesticides,  
Biocides



## In vitro Efficacy

- Tissue-healing
- Photo-protection
- Anti-inflammation / Calming
- Anti-sensitization effect
- Anti-adipogenesis & slimming
- Pigmentation & whitening
- Anti-ageing
- Antipollution
- Anti-oxidant
- Permeation enhancement
- Barrier function & hydratation
- Matrix composition & synthesis



## In vitro Toxicology

### DRUG-DRUG INTERACTIONS / LIVER, INTESTINAL, RENAL [FDA Compliance]

#### Victims

- CYP450 and UGT phenotyping
- Uptake and Efflux transporter substrate

#### Perpetrators

- CYP450 induction
- CYP450 and UGT inhibition
- Uptake and Efflux transporter inhibition
- Bile Salt Export Pump (BSEP) inhibition



## In vitro ADME

### ORAL ABSORPTION

- Caco-2 or 3D Human Intestinal models
- Biowaivers for generics *FDA Compliance*
- Performance of oral formulations

### CUTANEOUS ABSORPTION

- Human skin, OECD 428
- 3D Human epidermis models
- Distribution

### SUB-LINGUAL PERMEABILITY

- Cell lines : HO-1-u-1
- 3D Human Oral Epithelium models

### IN VITRO METABOLISM

- Liver, GI fluids, Plasma, Cutaneous

### MET-ID

- Metabolite identification / HR-Mass

### PROTEIN BINDING

### DRUG INDUCED LIVER INJURIES (DILI)

- NASH in vitro assays
- Biomarkers monitoring: MCFAs

### MUCOSAL IRRITATION / CORROSION

- Skin irritation, OECD 439
- Skin corrosion, OECD 431
- Ocular irritation, OECD 492
- Other mucosae

### SKIN SENSITIZATION

- DPRA – MSMS, OECD 442C
- SENSIL-18 (RhE\*/IL-18)
- KeratinoSens™, OECD 442D
- h-CLAT, OECD 442E
- GARD assay, OECD 442E<sup>New</sup>

### SKIN PHOTO – TOXICITY/SENSITIZATION

- Phototoxicity on 3T3 NRU, OECD 432
- Phototoxicity on RhE\*, OECD 498
- Photo-sensitization

### GENOTOXICITY

- AMES assay, OECD 471
- Micronucleus assay, OECD 487
- Micronucleus 3D assay with RhE\*

\*RhE : reconstructed human epidermis

## Bioanalytical support (Including GLP)

- Method Development up to validation
- HR-MS ; LC-MS/MS ; RT-qPCR ; UV ; Fluorescence ; Luminescence ; ELISA
- Analytical support to *in vitro*, PK and TK Studies

## Marketing : Ready to use Caco-2 TC7 plated cells

- License from INSERM Transfert

## Complex mixture testing

- Botanical and microbiota extracts