

**DEVELOPMENT OF NATIONAL CAPACITIES FOR THE  
IMPLEMENTATION OF ALTERNATIVE METHODS:  
A NEW CHALLENGE IN URUGUAY**

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# Institut Pasteur International Network (RIIP)



In 2009: NATIONAL LAW 18.611

PROCEDURES FOR THE USE OF ANIMALS IN EXPERIMENTATION,  
TEACHING & RESEARCH ACTIVITIES



NATIONAL COUNCIL OF ANIMAL EXPERIMENTATION



- Register Qualified Institutions
- Ethics Committee on the Use of Animals (each institution)
- National System of Personal Accreditations

# Institutional programs - “One health” concept

**Animal Health**, zoonotic diseases or microbiology.

**Genomics**, including human and medical genomics, pathogen genomics.

**Human Health**

**INDICYO**. Inflammatory & metabolic diseases.

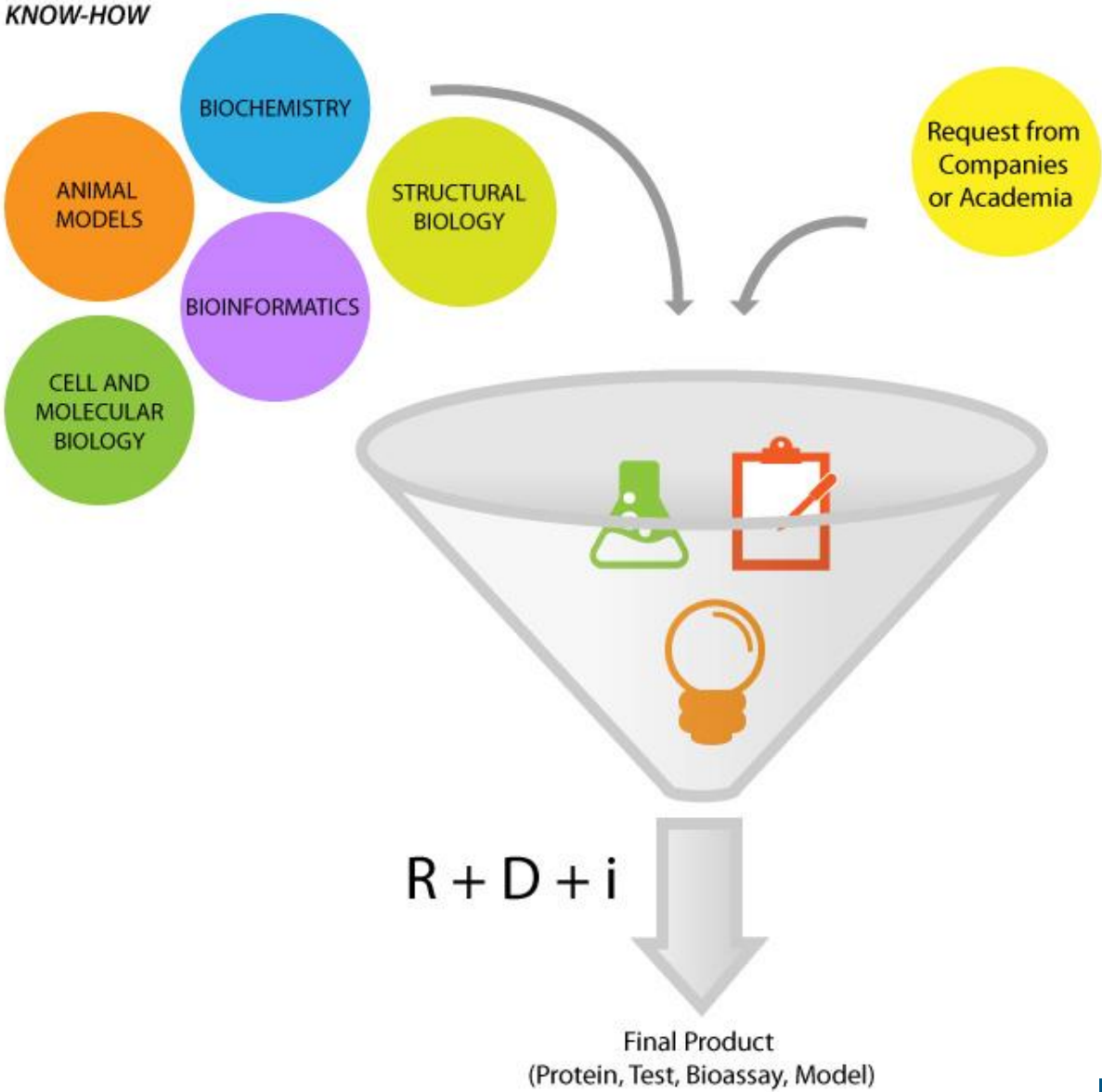
**Cancer Immunology**

**Biotechnology**

**PROTEMCA**. Molecular, Cellular & Animal Technology.

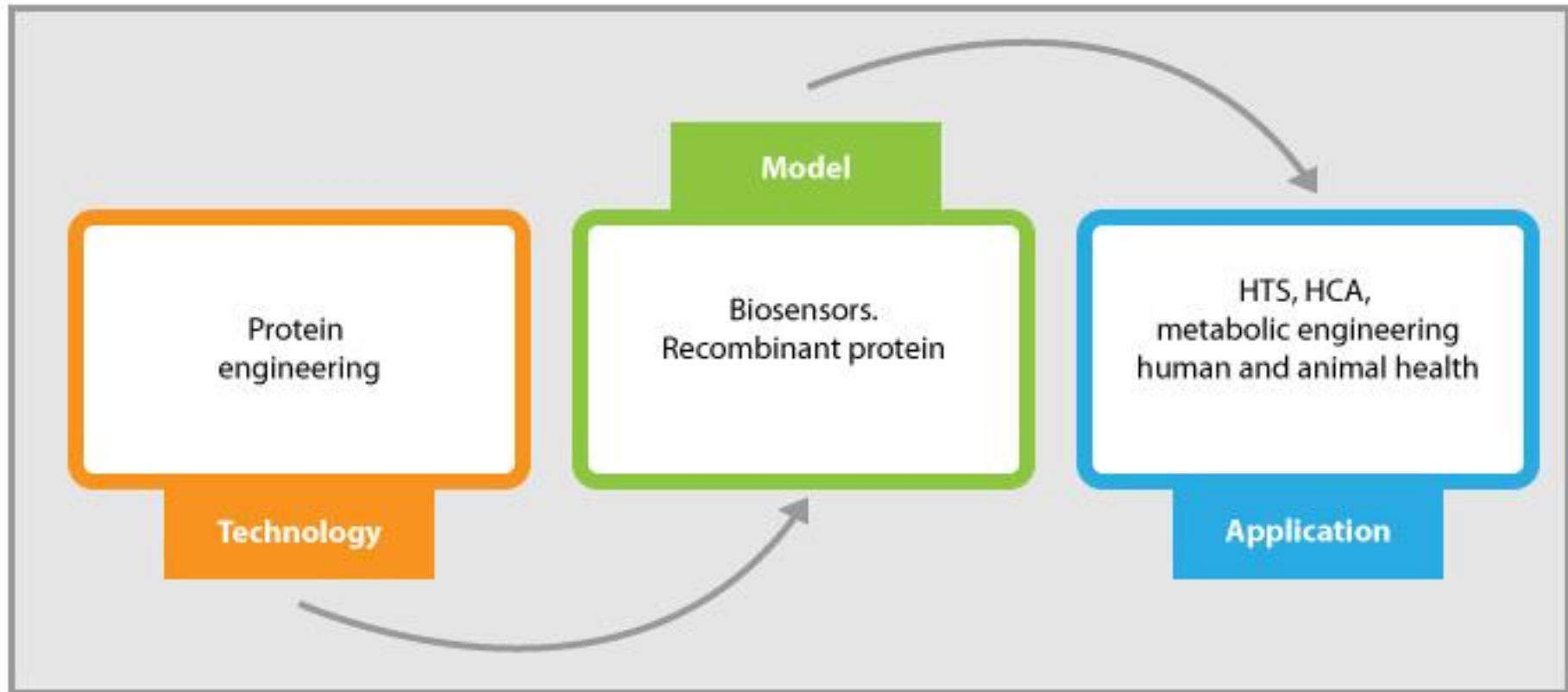


ProTeMCA: Founded in 2015





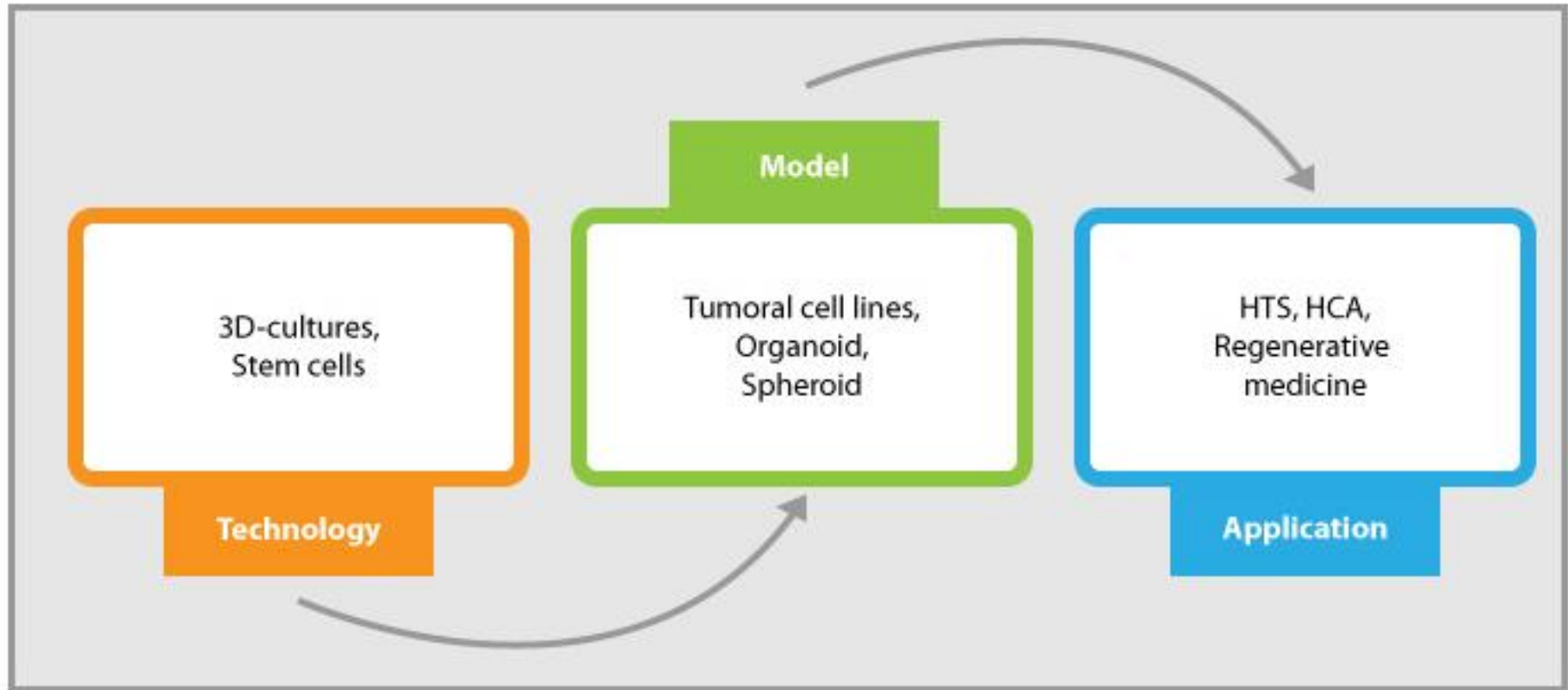
## 1. Design & refinement of products of biotechnological interest



HTS: *Hight - throughput screening*  
HCA: *High content analysis*



## 2. Development of new cell-based assays for HTS, HCA & toxicology studies

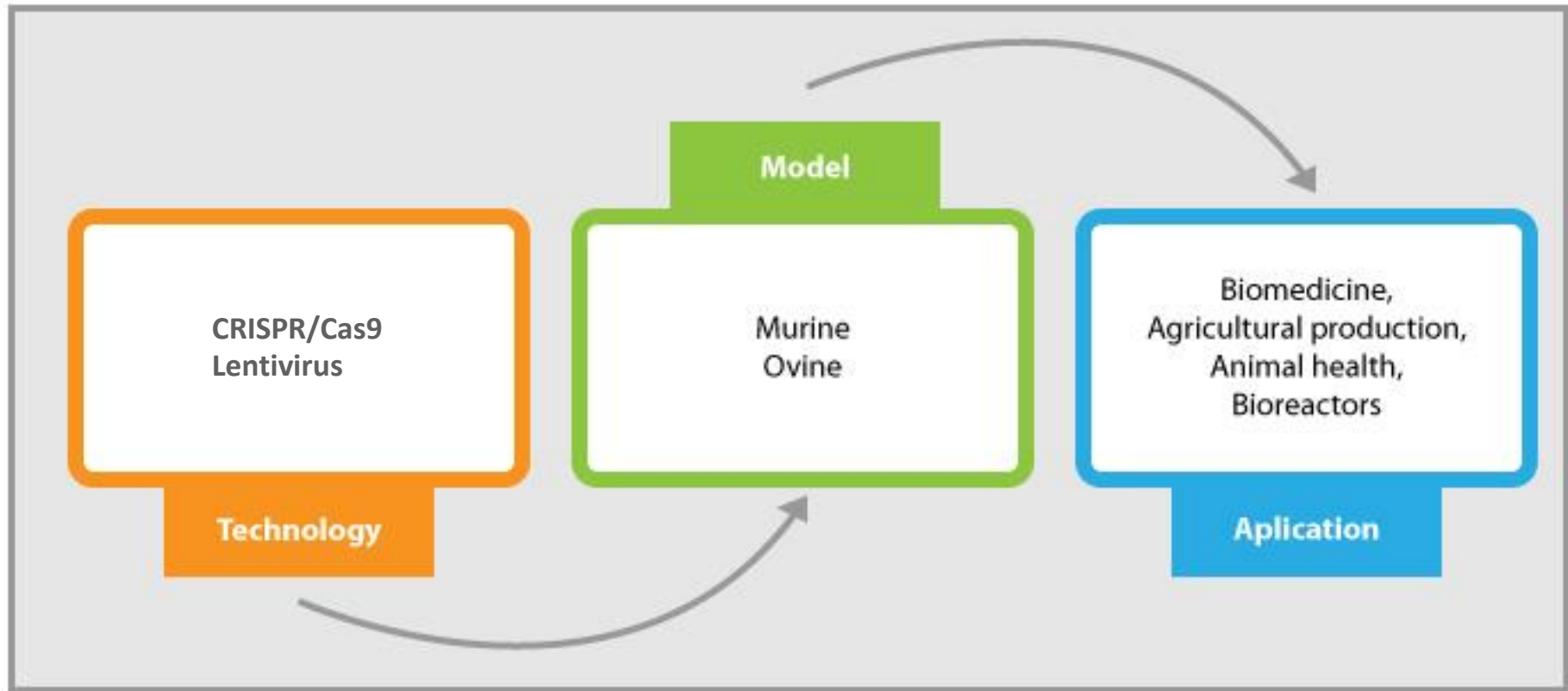


**Implementation of Alternative Methods**

HTS: *Hight - throughput screening*  
HCA: *High content analysis*



## 3. New animal models for toxicological and disease studies



**Implementation of 3R**





## DEVELOPMENT OF NATIONAL CAPACITIES FOR THE IMPLEMENTATION OF ALTERNATIVE METHODS (2017)

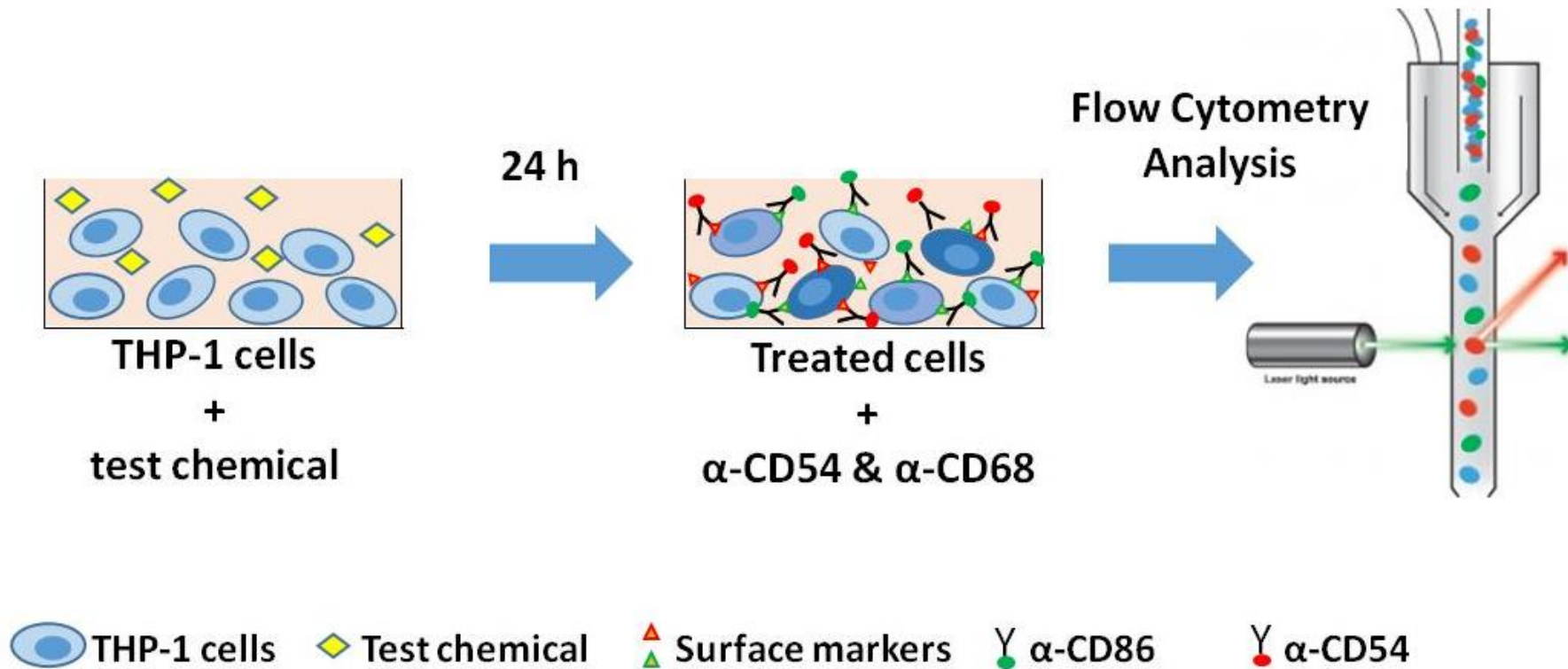
- ✓ To implement a quality management system (GLP lab, documentation)
- ✓ To implement validated OECD protocols for toxicology allowing the **REDUCTION** or **REPLACEMENT** of experimental animals
- ✓ To train HR in the application and validation of **Alternative Methods**
- ✓ To deliver national and regional training courses on **Alternative Methods**
- ✓ To advice regulatory agencies on the uses of **Alternative Methods**

# IMPLEMENTATION OF OECD TG 442E



## In vitro skin sensitization test:

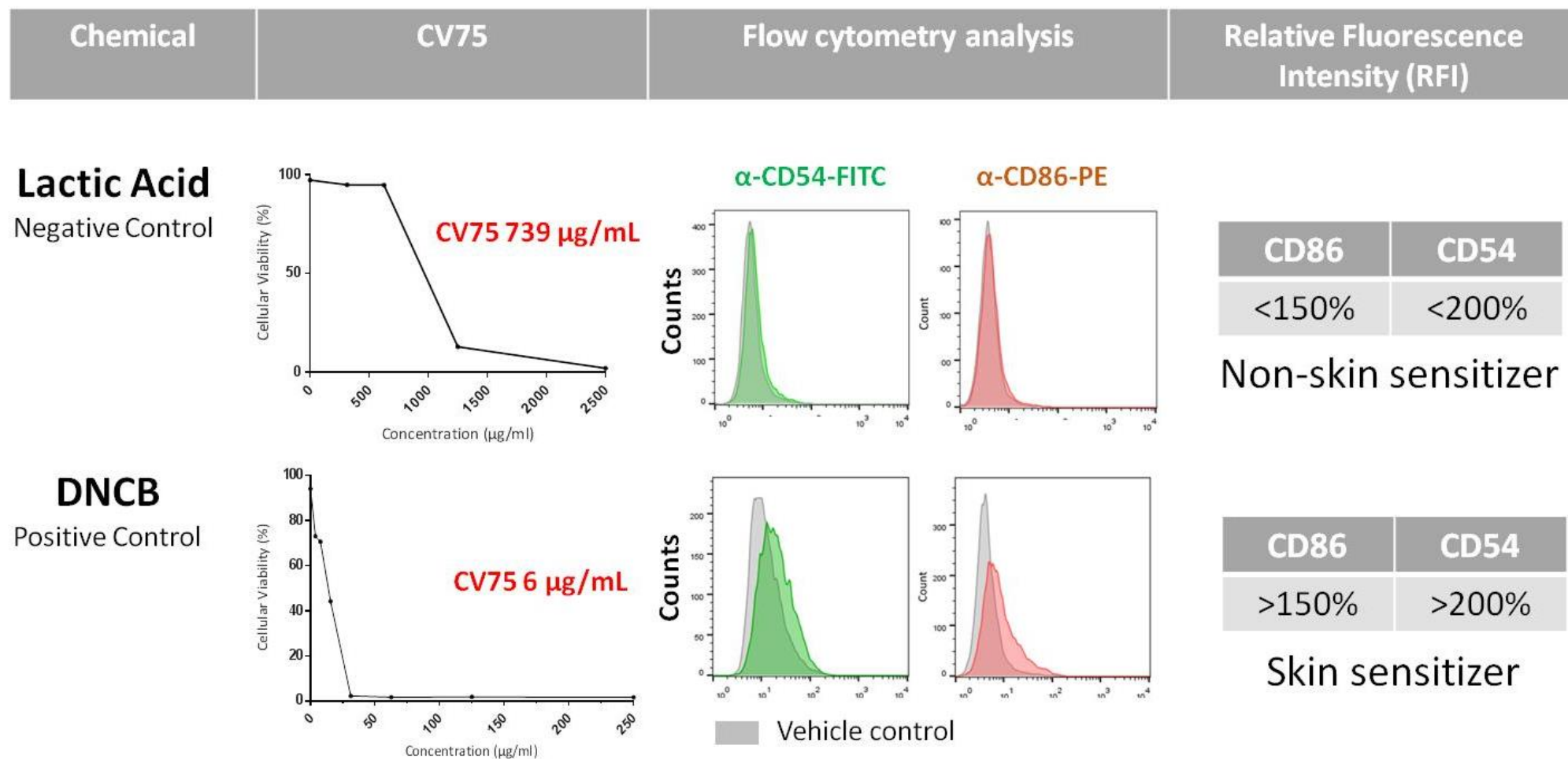
OECD TG 442E: human Cell Line Activation Test (h-CLAT)



# IMPLEMENTATION OF OECD TG 442E



Examples of two substances used as positive and negative skin sensitization controls.

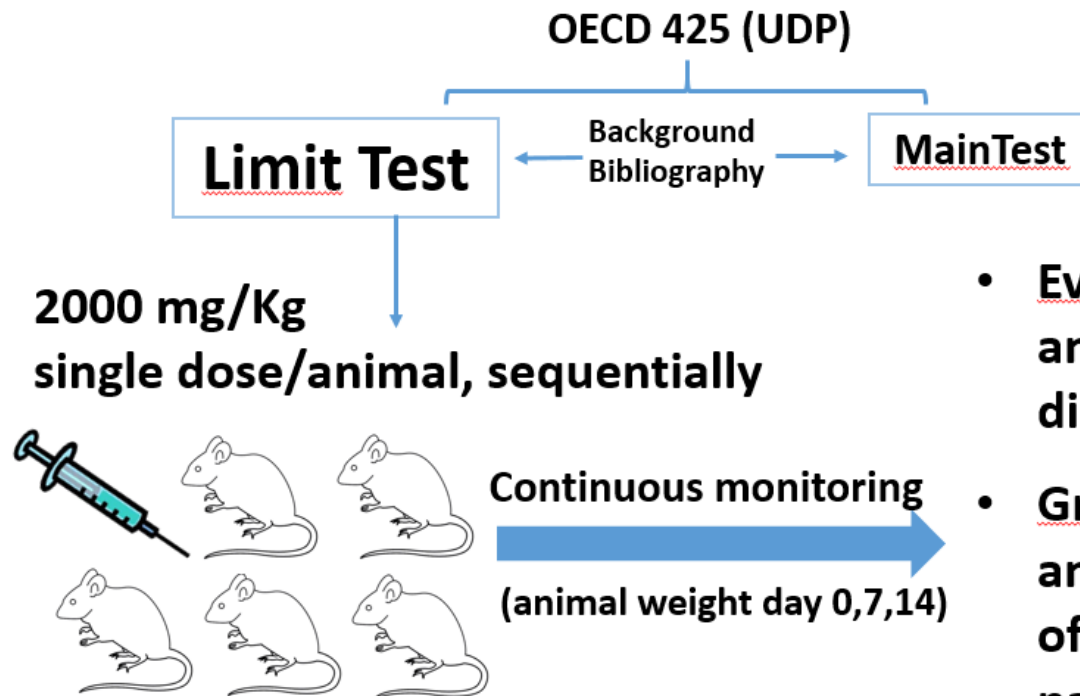


# IMPLEMENTATION OF OECD 425



## In vivo Acute Oral Toxicity:

Up and Down Procedure. Two strains of soil bacteria were used



- Evaluation of parameters for animal welfare score. If  $\geq 3$  animals die, conduct the Main Test
- Gross necropsy performed in every animal, microscopic examination of organs if evidence of gross pathology
- If  $\geq 3$  animals survive, LD50 is greater than 2000 mg/kg



## **Annual training course**

Ethic Use of Experimental Animals

## **February 2017**

Hands on training course: XTREME-Bruker *in vivo* technology

# TRAINING COURSES



**October 2017**

International course: Cell and Animal Models for Drug Discovery



European Society for Animal Cell Technology





# TRAINING COURSES



# FINAL REMARKS



- ✓ Quality management system is implemented
- ✓ Two OECD validated tests are implemented:
  - OECD TG 442E (hCLAT)
  - OECD Test 425
- ✓ Different training courses were delivered
- ✓ Uruguayan Regulatory Agencies & Companies start to discuss on the implementation of alternative methods



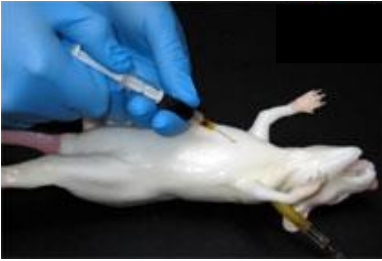


To implement new OECD protocols for toxicological studies

<b>SKIN</b> <i>In chemico, in vitro</i>	<b>OCULAR</b> <i>In vitro</i>	<i>In vivo</i>
OECD TG 442C (Direct Peptide Reactivity Assay)	OECD TG 437 (Bovine cornea opacity & permeability)	OECD TG 402 (Acute Dermal Toxicity)
OECD TG 442D (KeratinoSens™)	OECD TG 460 (Fluorescein Leakage, MDCK)	OECD TG 403/436 (Acute Inhalation Toxicity)
OECD TG 442E (U-SENS™)		
OECD TG 439 (Reconstructed Human Epidermis)		



To introduce silicone animal models for training courses



To install In-Vivo XTREME II system (Bruker)

To develop new cell-based assays

To become center of reference in Uruguay

To establish collaborations outside Uruguay



# THANK YOU



**Cecilia Abreu**

**Constanza Silvera**

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**Sergio Pantano**

**Marcelo Comini**



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