

Uso de animais em estudos pré-clínicos

Luciana Cintra

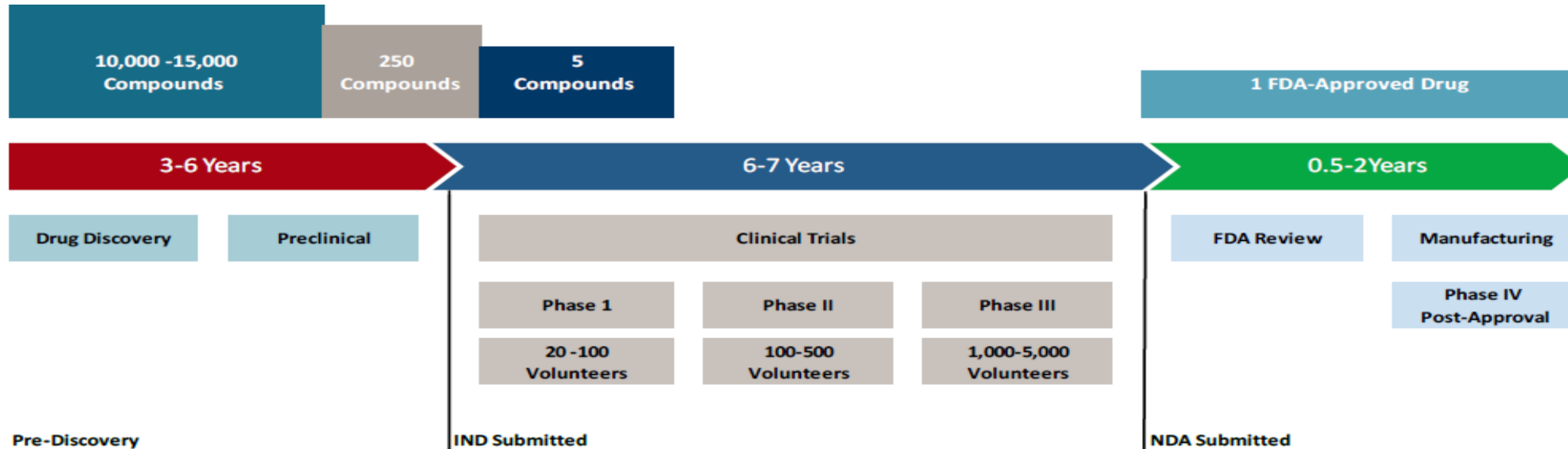


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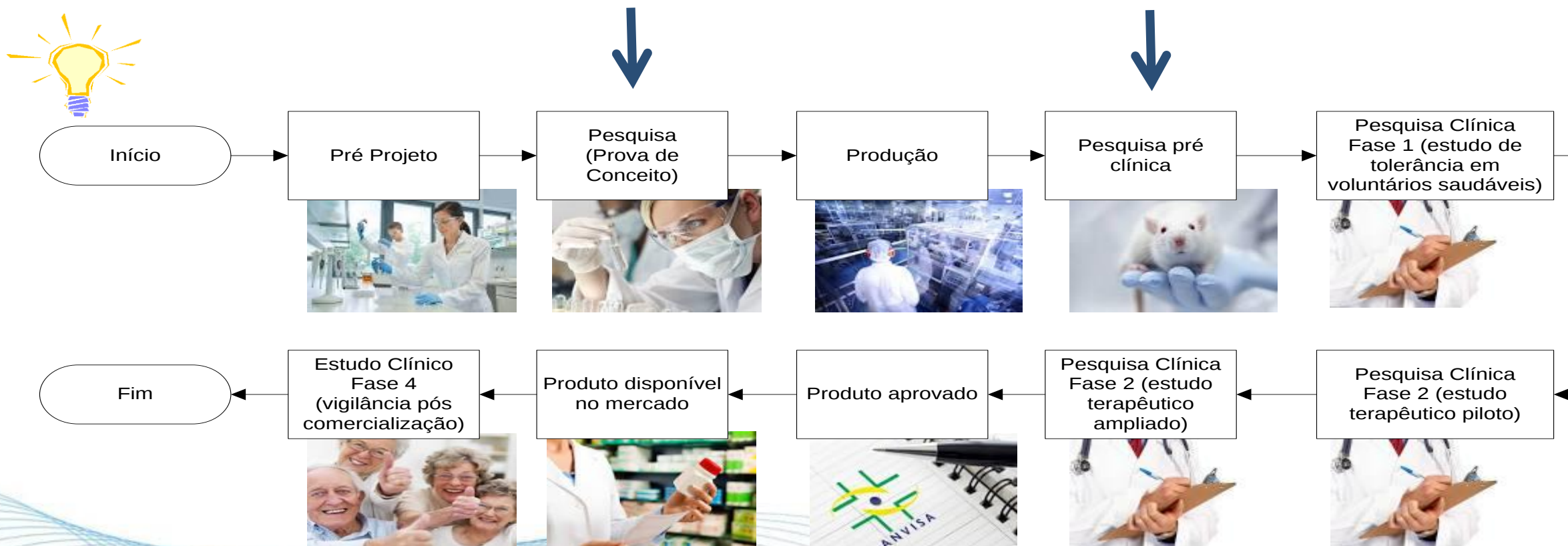
16/10/2020

Fases para validação de um produto na área saúde



Fonte: FDA, Credit Suisse

O que envolve o estudo pré-clínico?



A pesquisa básica em medicamentos inclui todas as atividades necessárias para a identificação e a validação do alvo terapêutico e das moléculas candidatas. Os testes pré-clínicos, realizados em laboratório (*in vitro*) ou em animais (*in vivo*), buscam determinar se a molécula é segura e eficaz o suficiente para iniciar os testes em humanos.

BNDES Setorial 36, p.45-84. Ensaios clínicos no Brasil: competitividade internacional e desafios, 2012.

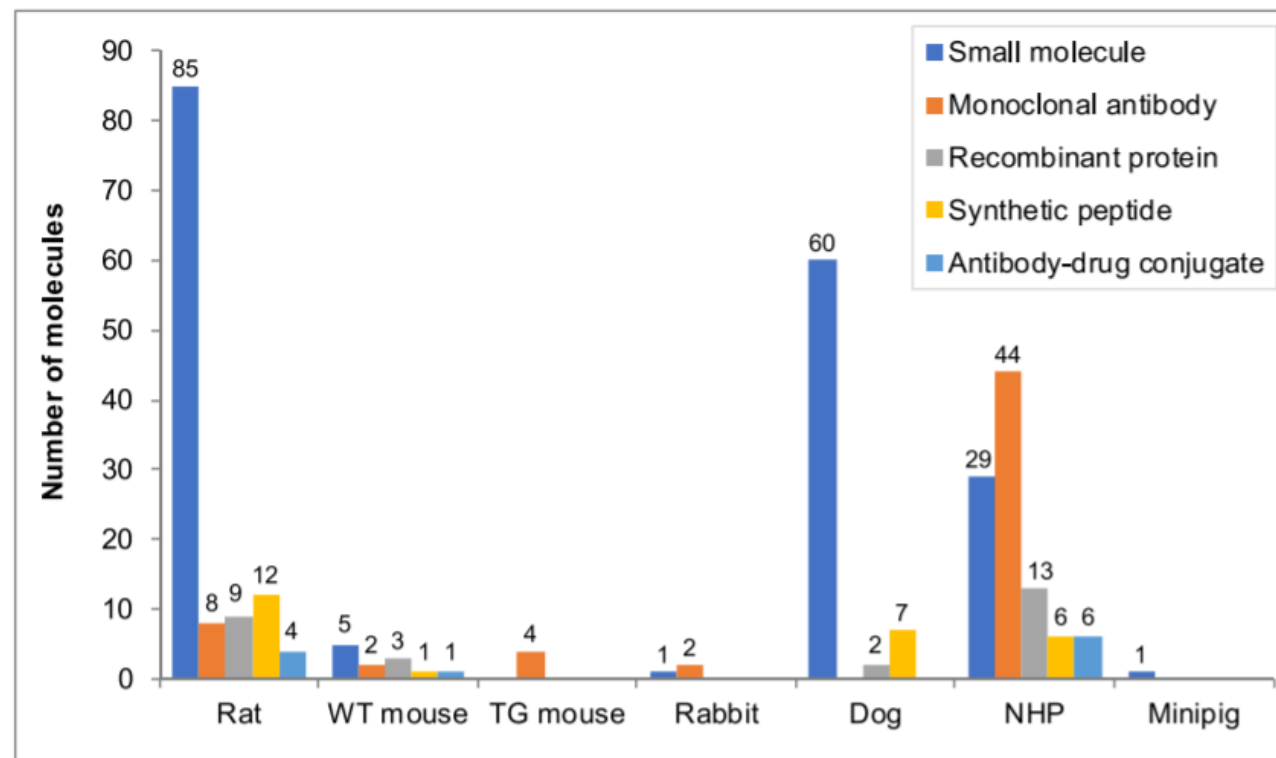


PAPER

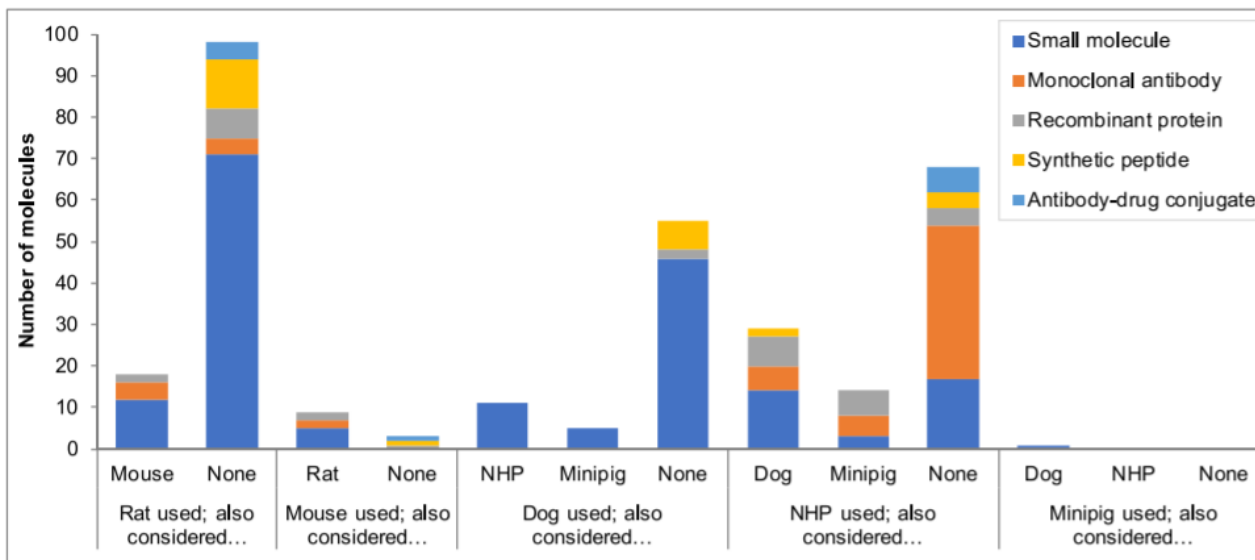
Justification for species selection for pharmaceutical toxicity studies

Helen Prior,^{1,*} Richard Haworth,² Briony Labram,¹ Ruth Roberts,³ Alison Wolfreys⁴ and Fiona Sewell¹

¹National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs), 215 Euston Rd, London, NW1 2BE, UK, ²GlaxoSmithKline R&D, Park Road, Ware, SG12 0DP, UK, ³Apconix, Alderley Park, Alderley Edge, SK10 4TG, UK and ⁴UCB Biopharma, Bath Rd, Slough, SL1 3WE, UK

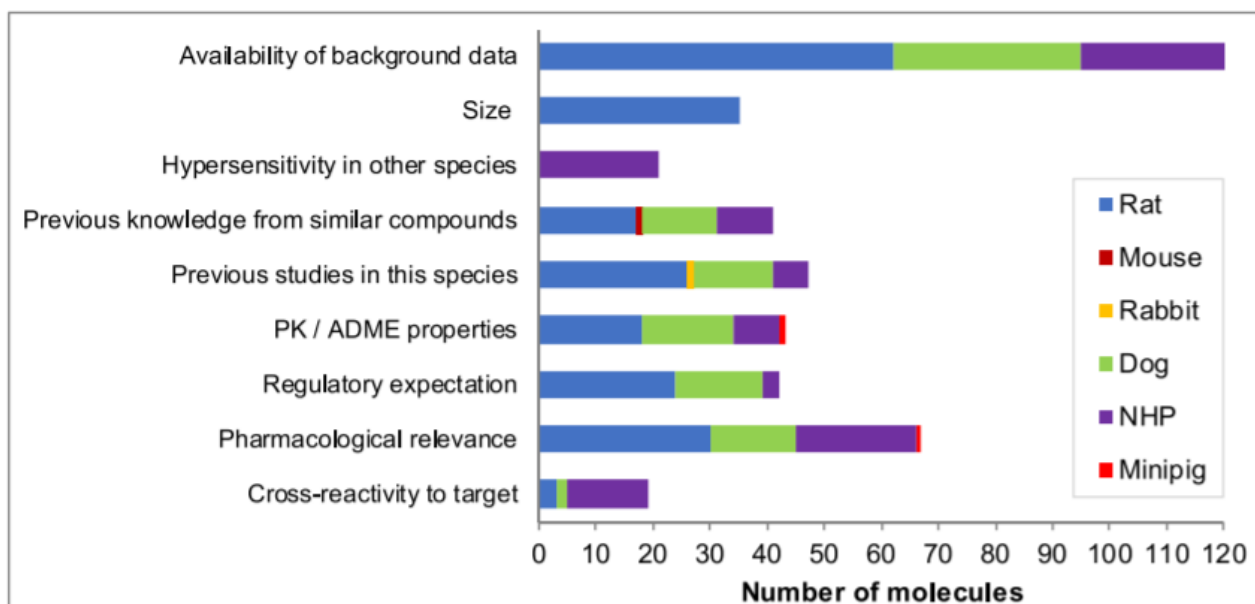


- International regulatory guidelines outline recommendations for the order (rodent and/or non-rodent)
- Toxicity assessments in animals form an integral part of the drug development process, providing data to support the design of human clinical trials and the safety of participating volunteers and patients.
- General toxicology, safety pharmacology, genetic toxicology, developmental and reproductive toxicology, carcinogenicity.
- Absorption, distribution, metabolism and excretion (ADME), safety pharmacology and genotoxicity, many components of regulatory general toxicology assessments rely on data from animals and are likely to do so for the foreseeable future, until reliable alternatives are available and widely accepted as replacements for animal use.



When is the minipig the relevant non-rodent toxicology species? (Richard Haworth, GSK)

- Many companies are considering the minipig as an alternative to dogs for small molecule development and also to reduce the use of NHPs.



Quais as vantagens e desvantagens desta espécie?

Qual o meu produto?



O que vou precisar para a validação do meu produto?



MODELO ADEQUADO

OECD Guidelines for the Testing of Chemicals



The OECD Test Guidelines Programme

The OECD Guidelines are a unique tool for assessing the potential effects of chemicals on human health and the environment. Accepted internationally as standard methods for safety testing, the Guidelines are used by professionals in industry, academia and government involved in the testing and assessment of chemicals (industrial chemicals, pesticides, personal care products, etc.). These Guidelines are regularly updated with the assistance of thousands of national experts from OECD member countries. OECD Test Guidelines are covered by the Mutual Acceptance of Data, implying that data generated in the testing of chemicals in an OECD member country, or a partner country having adhered to the Decision, in accordance with OECD Test Guidelines and Principles of Good Laboratory Practice (GLP), be accepted in other OECD countries and partner countries having adhered to the Decision, for the purposes of assessment and other uses relating to the protection of human health and the environment.

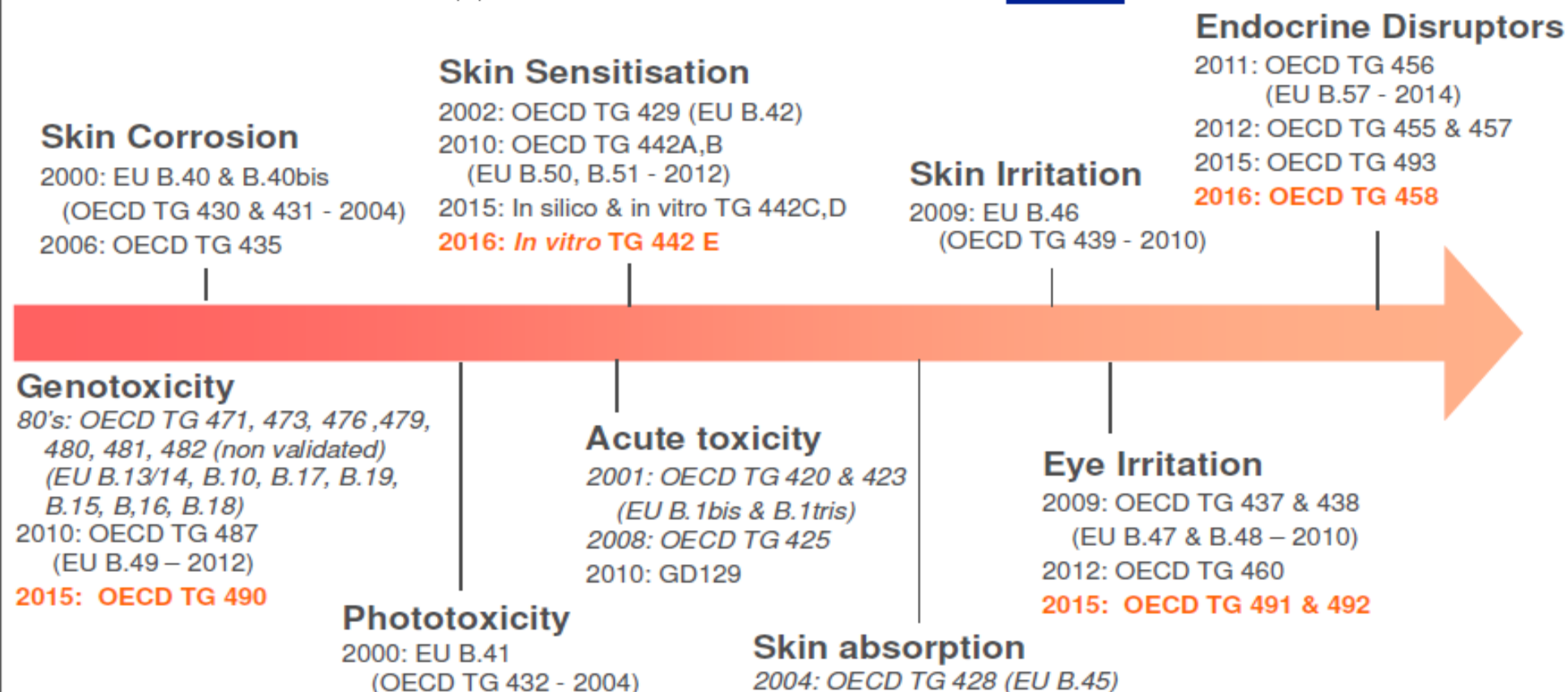
- › [Section 1: Physical Chemical Properties](#)
- › [Section 2: Effects on Biotic Systems](#) (Software for TG 223)
- › [Section 3: Environmental Fate and Behaviour*](#) (Softwares for TG 305 and TG 318)
- › [Section 4: Health Effects](#) (Software for TG 455, TG 432 and TG 425)
- › [Section 5: Other Test Guidelines](#)



Monitoramento BPL

International Acceptance of Alternative Methods

OECD  Chemicals 



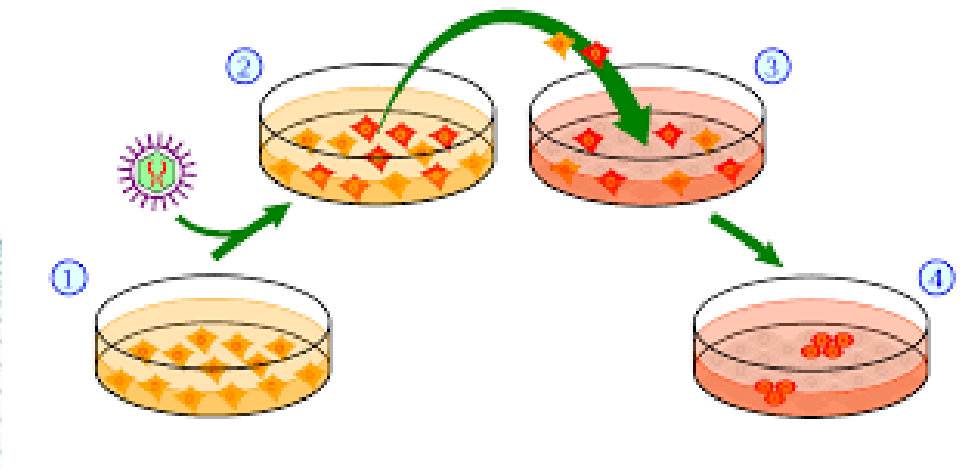
Métodos alternativos estudos dermatológicos



3D models

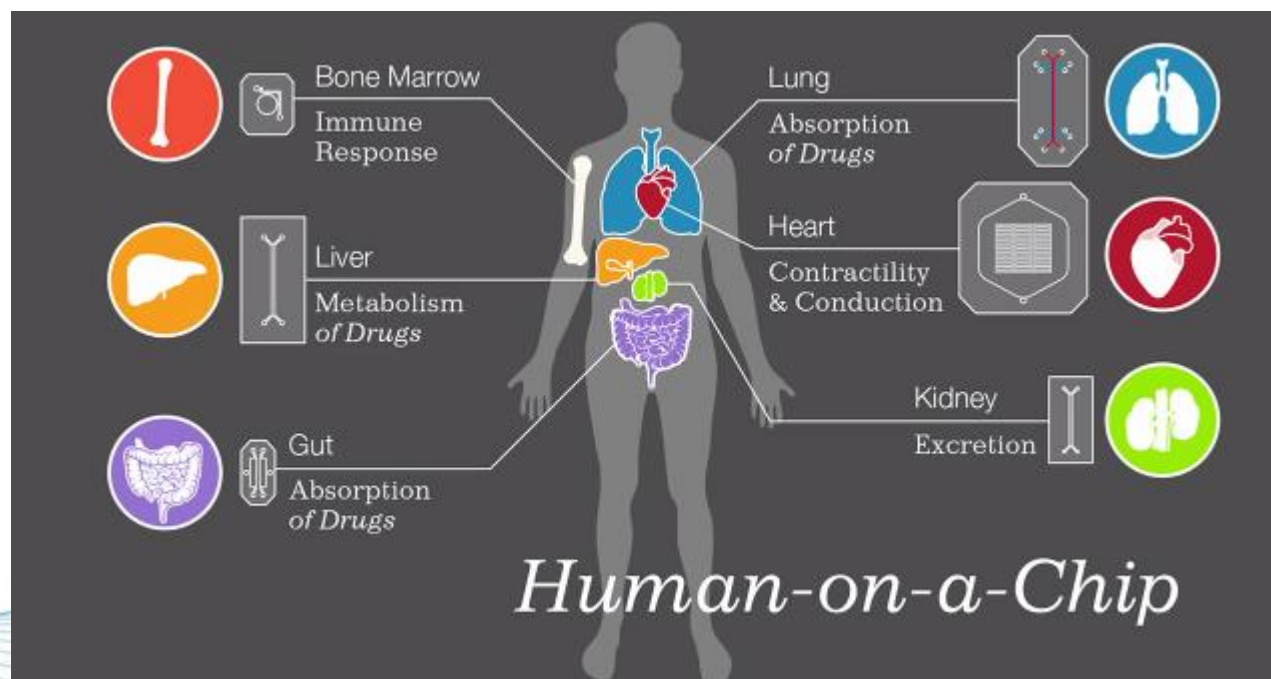
MODELS	APPLICATIONS
 T-Skin Human Full Thickness Model	☐ ☐ ☐ ☐ ☒ ☒ ☒ ☒ ☒ ☐ ☐
 SkinEthic RHE Human Epidermis	☒ ☐ ☐ ☒ ☒ ☒ ☒ ☒ ☒ ☐ ☐
 EpiSkin Human Epidermis	☒ ☐ ☐ ☒ ☒ ☒ ☒ ☒ ☒ ☐ ☐
 SkinEthic RHPE Pigmented Epidermis	☐ ☐ ☐ ☐ ☒ ☐ ☐ ☒ ☐ ☒ ☐
 SkinEthic HCE Corneal Epithelium	☐ ☐ ☐ ☐ ☐ ☒ ☐ ☒ ☐ ☐ ☒
 SkinEthic HOE Oral Epithelium	☐ ☒ ☐ ☐ ☐ ☒ ☐ ☒ ☐ ☐ ☐
 SkinEthic HGE Gingival Epithelium	☐ ☒ ☐ ☐ ☐ ☒ ☐ ☒ ☐ ☐ ☐
 SkinEthic HVE Vaginal Epithelium	☐ ☐ ☒ ☐ ☐ ☒ ☐ ☒ ☐ ☐ ☐

- **Células-tronco pluripotentes induzidas (IPSC):** estas células representam uma grande promessa para a medicina, uma vez que, tendo a capacidade de se diferenciar em qualquer tecido de um organismo adulto, dão esperança de que um dia seja possível reconstruir tecidos ou órgãos de pacientes e ainda auxiliar no desenvolvimento de fármacos para as mais diferentes moléstias humanas.



Inovação em estudos pré-clínicos

- Human on a chip



Desafios na extrapolação de dados dos animais aos seres humanos: estudos em imunologia, sistema nervoso central e oncologia.

Serviços disponíveis no mundo



Are You Looking for a Preclinical CRO with Proven Cardiovascular, Neurovascular and Peripheral Vascular Experience?

We can help. Surpass has assisted hundreds of companies advance their vascular innovations through preclinical research.

IMAVITA is an **innovating contract research organization** proposing **preclinical services** in the **exploration of preclinical models** of human pathologies by the use of **innovating imaging techniques**.

The vision of our company is to propose to **pharmaceutical industries, biotechnology companies and other private & public laboratories**, innovating solutions in **efficacy / toxicity evaluation of active ingredients** in laboratory species by the use of non invasive imaging techniques and appropriate imaging analysis for quantitative evaluation of specific imaging biomarkers.

IMAVITA is actually developing the following **tools**:

- ⦿ **Pre-clinical services** testing in laboratory species (induction of pathologies / treatment & sampling phases)
- ⦿ **Imaging techniques** like SPECT/CT, CT with Single/Dual Energy CT approach, MRI, ultrasonography, etc...
- ⦿ **Images exploitation and analysis** for quantitative imaging



Home About Us Expertise

Who We Are



Pharma Models is a pre-clinical contract research organization based in eastern Massachusetts conveniently close to the Boston and Worcester metro areas.

We specialize in animal models of human diseases in the areas of **cancer research, inflammatory**

diseases, obesity and diabetes. Every study we perform is a custom designed study, tailored specifically for the intended client and designed to meet specific needs. Let us design a study for you today.

Pharma Models is owned entirely by the scientists that work here and is committed to providing quality services to the pharmaceutical industry at eminently affordable prices.

Applications of Imavita services:

- ⦿ **Dermatology**
- ⦿ **Oncology**
- ⦿ **Drug disposition / PK**
- ⦿ **Medical Devices**
- ⦿ **Osteo-articular**
- ⦿ **Cardiovascular**

Linhas de Estudos - Modelos de avaliação de eficácia *in vivo*



Neurologia

Avaliação de memória.

Ansiedade e depressão.

Epilepsia.

Modelo de Acidente Vascular Cerebral.

- Modelo de isquemia cerebral focal e global

Modelo de doença de Parkinson induzida por 6-OHDA.



Oncologia

Modelo de Glioblastoma cerebral.

Modelo de tumores ectópicos

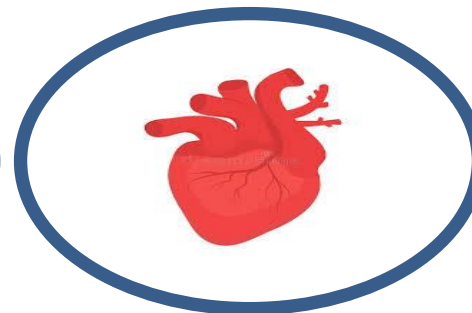
- Câncer de próstata.



Hematologia

Modelo xenogênico de Leucemia Mielóide Aguda

Modelo xenogênico de Leucemia Mielóide Aguda



Cardiologia

Registro de ECG e imagens cintilográficas de ventriculografia radioisotópica.

Imagens tomográficas SPECT de coração de ratos.

Modelo de infarto do miocárdio

Modelo de hipertensão arterial.



Distúrbios metabólicos

Modelo patológico de obesidade e diabetes (camundongo ObOb).

Diabetes induzida pela estreptozotocina.

Obesidade induzida por dieta hipercalórica

Modelo patológico de aterosclerose (camundongos APOE).

Infraestrutura do CETEC



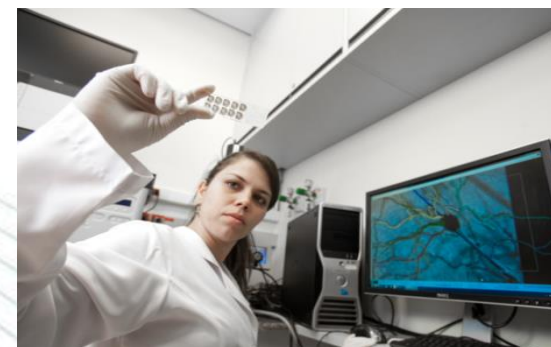
Salas cirúrgicas para estudos em animais de médio porte: suínos, coelhos e pequenos ruminantes.



Laboratório de patologia
experimental

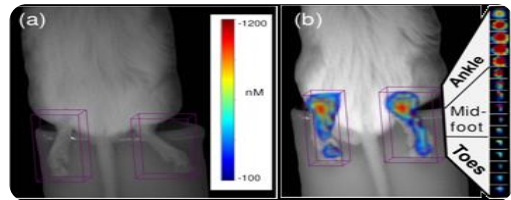


Laboratório de
radiofarmácia

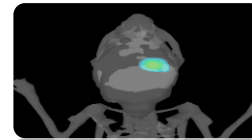


Microscópio motorizado de fluorescência

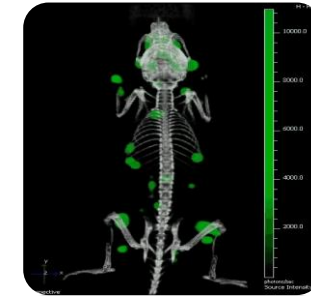
AVALIAÇÃO DE PATOLOGIAS (*in vivo*)



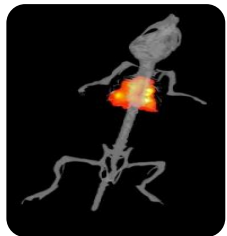
Inflammation



Neuroscience



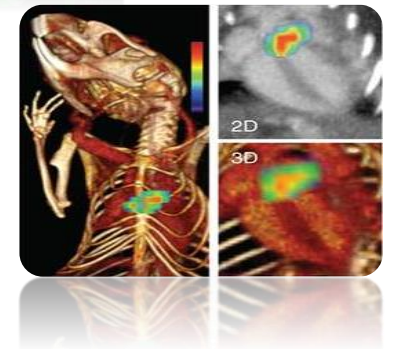
Oncology



Infectious diseases

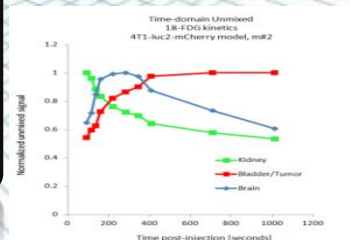
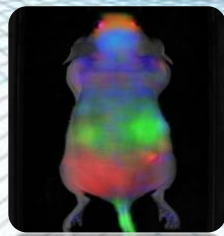


Cardiovascular

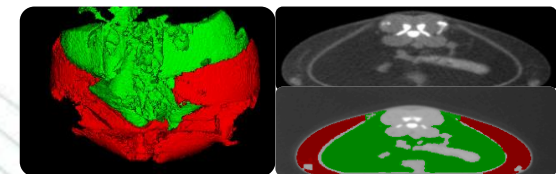
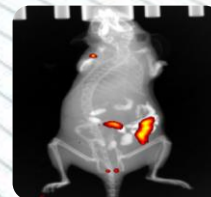


Metabolic Disorders

*Biodistribution
PK/PD*



Gastrointestinal



Estudos de Segurança Farmacológica

Estudos	# OECD Test	OECD Guidelines for the Testing of Chemicals	Modelo
Estudos de toxicidade de dose única (aguda)	420	Acute Oral Toxicity – Fixed Dose Procedure	Ratos
Estudos de toxicidade de doses repetidas	407	Repeated Dose 28-Day Oral Toxicity Study in Rodents	Ratos
	408	Repeated Dose 90-day Oral Toxicity Study in Rodents	Camundongos
	409	Repeated Dose 90-Day Oral Toxicity Study in Non-Rodents	Mini-pigs
Estudos de toxicidade reprodutiva	421	Reproduction/Developmental Toxicity Screening Test	Ratos
Estudos de genotoxicidade (in vitro e in vivo)	471	Bacterial Reverse Mutation Test (in vitro)	S. typhimurium
	474	Mammalian Erythrocyte Micronucleus Test (in vivo)	Camundongos
Estudos de tolerância local	EMA	Guideline on non-clinical local tolerance testing of medicinal products	Ratos
Estudos de carcinogenicidade	453	Combined Chronic Toxicity/Carcinogenicity Studies	Ratos
Estudos de interesse para avaliação da segurança farmacológica		Sistema Nervoso Central	Ratos
		Sistema Cardiovascular	Coelhos
		Sistema Respiratório	Camundongos
Estudos de toxicocinética	417	Toxicokinetics	Ratos

Estudos em Neurociências

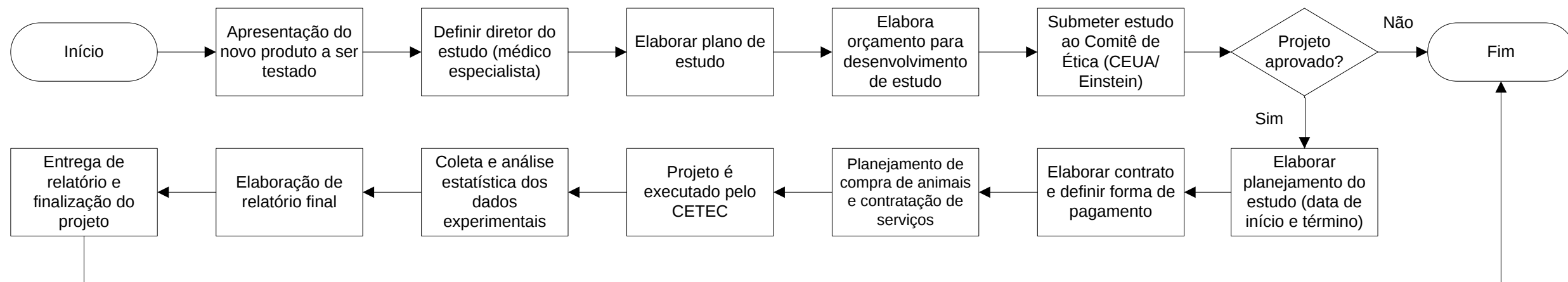
Estudos de Neuropatia

Estudos de Ansiedade e Depressão

- Campo Aberto
- Suspensão da cauda
- Plataforma em T ou Cruz Elevado
- Nado forçado
- Derrota social



Fluxo de Serviços Contratados



OBRIGADA

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