

GLP Certificate holder

# MEDITOX

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## PRECLINICAL RESEARCH AND DEVELOPMENT

cardiology, diabetes, neurology, vaccines, ophthalmology

## COMPREHENSIVE PRECLINICAL TOXICOLOGICAL PROGRAM

human and veterinary drugs, biological, medical devices, REACH

## ANIMAL MODELS OF SELECTED HUMAN DISEASES

CVS, neurodegenerative, ophthalmic, diabetes

## ACCREDITED BREEDING FACILITY FOR LABORATORY ANIMALS

non-human primates, dogs, rodents



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CARDIOLOGY DISEASES

HUNTINGTON'S DISEASE MODEL

DIABETES / OBESITY MODEL

OPHTHALMOLOGY DISEASES

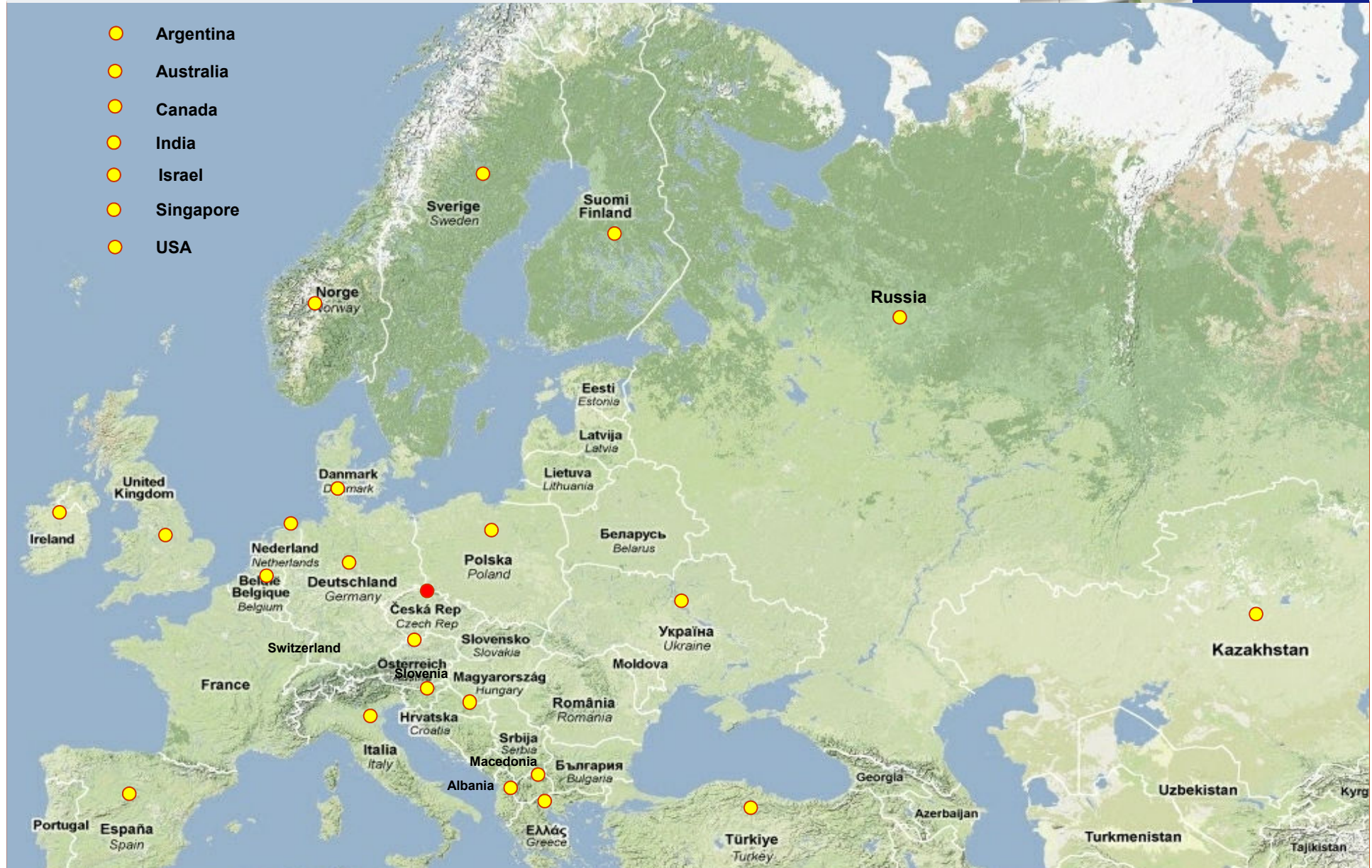


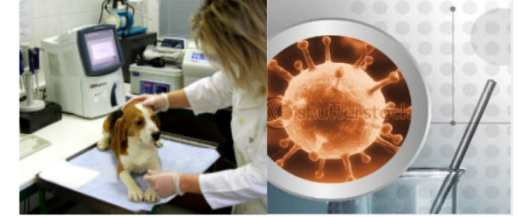
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- Argentina
- Australia
- Canada
- India
- Israel
- Singapore
- USA





## History

**1951: Research Institute for Pharmacy and Biochemistry, Prague**  
**250 drugs (29 original substances)**  
**Pelentan, Kebuzon, Dosulepin, Metipranolol**  
**Full chain of drug development**

**1999: Privatization and splitting off RIPB into several private companies - BioTest s.r.o.** (branch of pre-clinical toxicology)

**April 1, 2013: Change the brand to MediTox s.r.o.**



## Main activities

### Preclinical R&D

Cardiovascular disorders, diabetes, preclinical vaccine development  
neurodegenerative diseases, ophthalmic diseases, osteoarthritis

### Comprehensive toxicological program

Human & veterinary pharmaceuticals/biological, food additives, medical  
devices (PHARM) chemicals & agrochemicals (REACH)

### Animal models of selected human diseases

Experimental IM, glaucoma, diabetes type II, chronic SCI, osteoarthritis

### Laboratory animal breeding

Non-human primates, dogs

## Certification

### **Good Laboratory Practice Certificate OECD GLP**

**[C(97)186 Final]** Pharmaceuticals, medical devices and food additives  
(PHARMA)

### **Good Laboratory Practice Certificate OECD GLP [C(97)186 Final]**

Chemicals, agrochemicals (REACH)

### **Authorization for Using of Experimental Animals**

The Central Committee for Animal Protection of the Ministry of Agriculture

### **Authorization for Breeding of Experimental Animals**

The Central Committee for Animal Protection of the Ministry of Agriculture

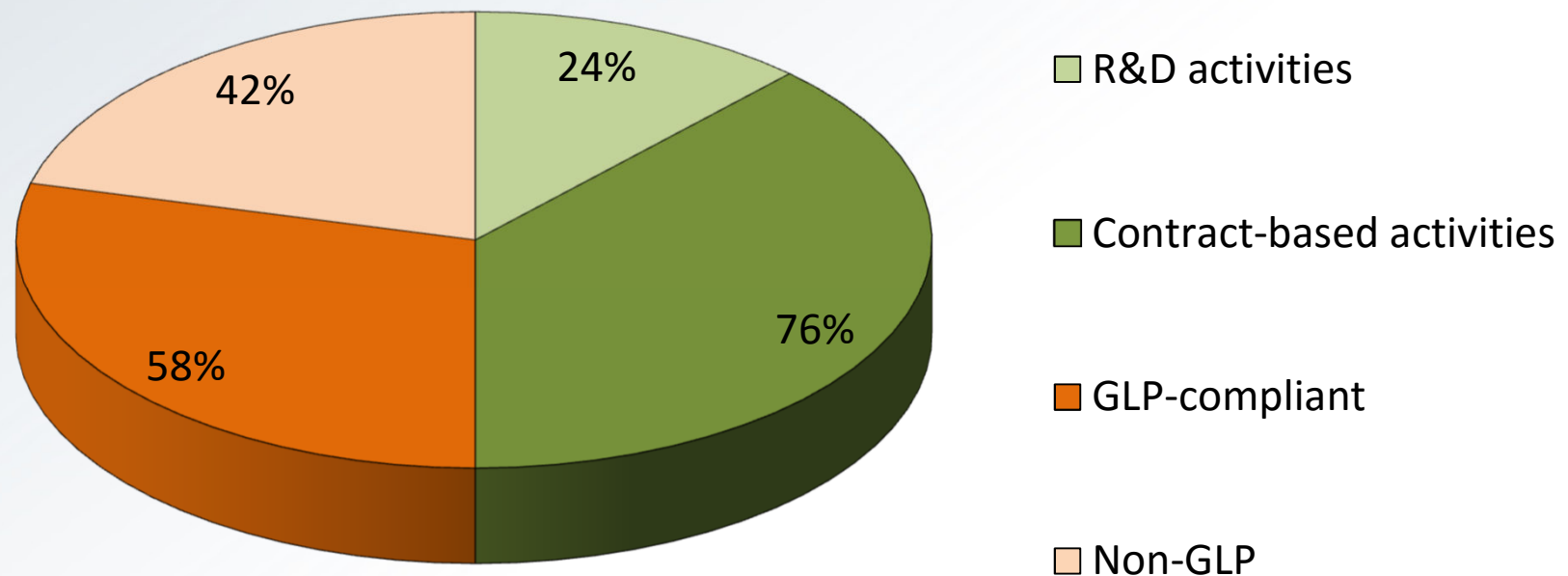
### **Approval for handling with GMO** in compliance with Act

No. 153/2000 Coll.



## Summary information

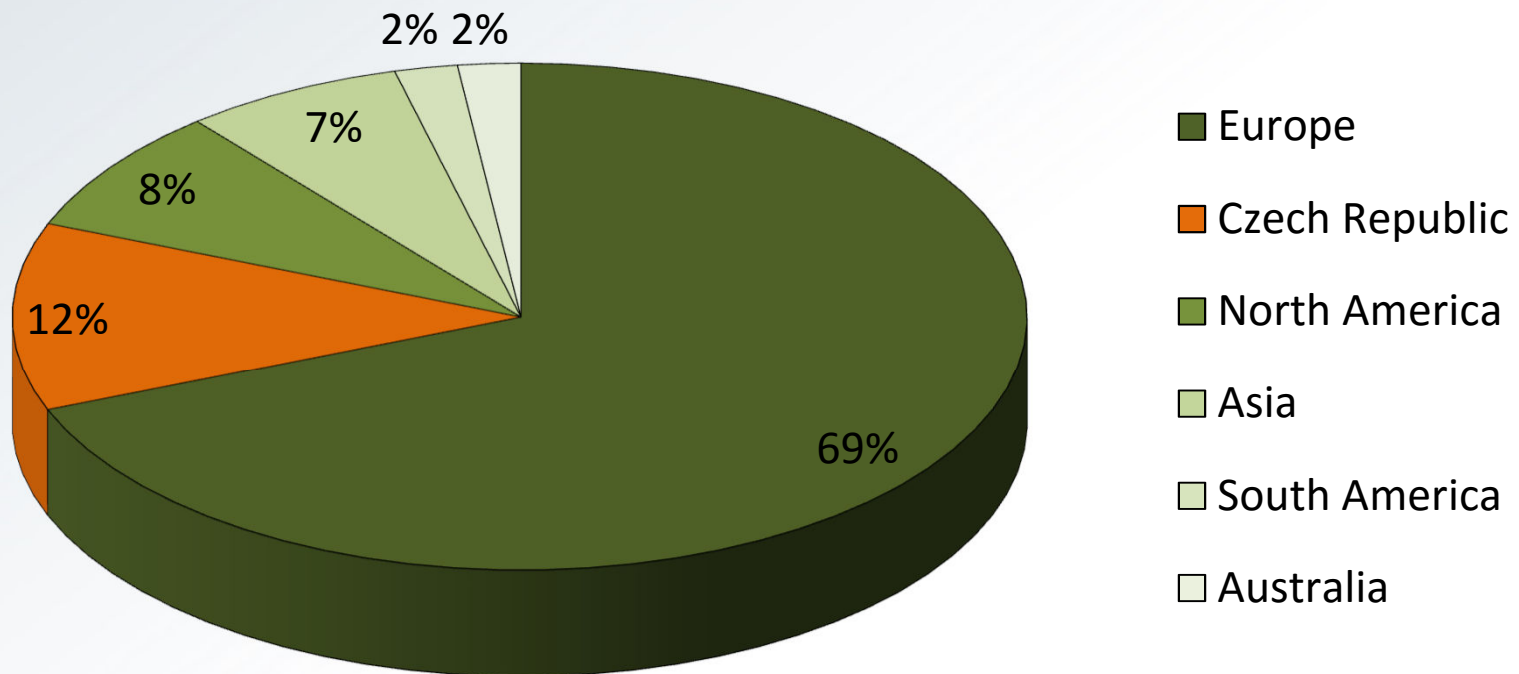
### Structure of experimental work





## Summary information

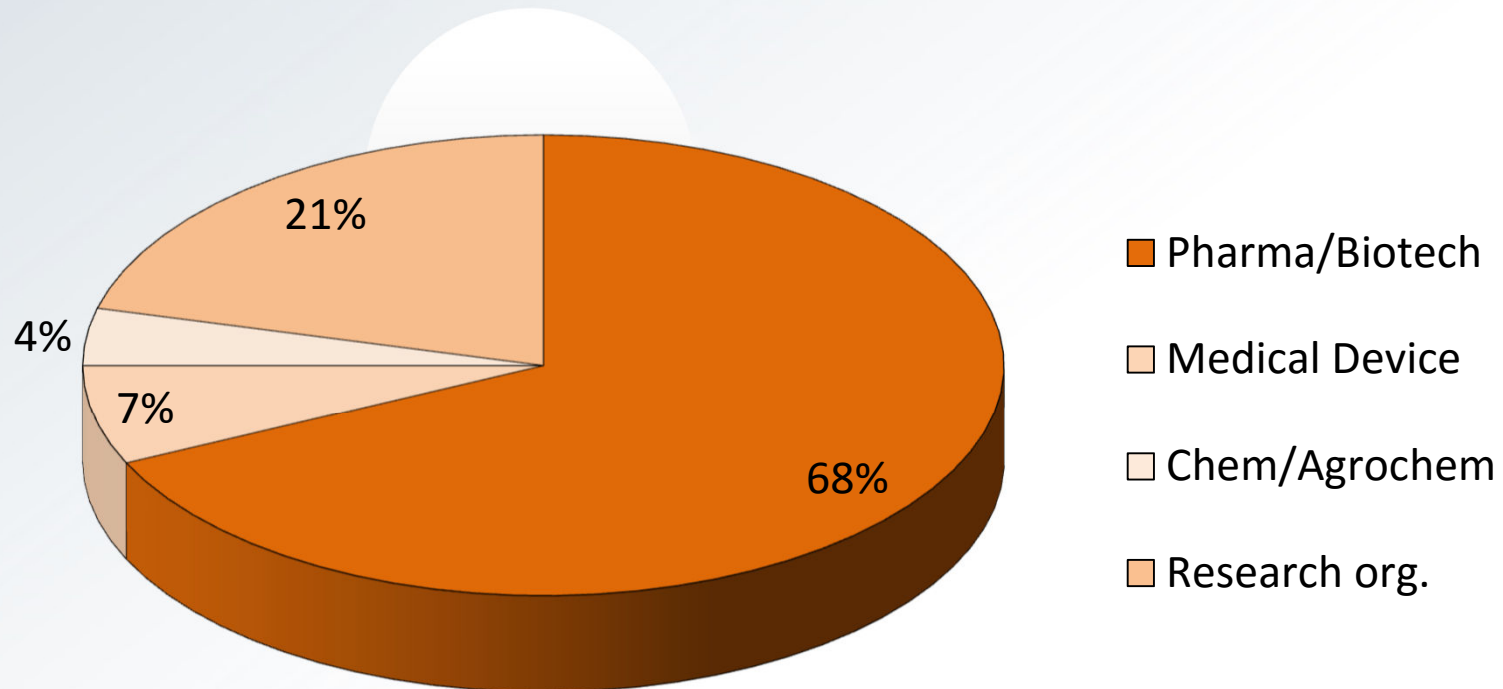
### Structure of clients





## Summary information

### Structure of clients







## R&D projects - international

### FLUVAC

**Live attenuated replication-defective influenza vaccine**

Austria (AGBT), Germany, Russia, Slovenia, Czech Republic

### ANTIFLU

**Innovative anti-influenza drugs excluding viral escape**

Denmark, France, Germany (MPI), Hungary, Israel, United Kingdom, Czech Republic

### OSTEOGROW

**Novel morphogenetic protein-6 biocompatible carrier device**

Austria, Bosnia and Herzegovina, Croatia (UZ), Czech Republic, Sweden

### MOTIF

**Micorbicide optimization through innovative formulation for vaginal and rectal delivery**

Czech Republic, France, Italy, United Kingdom (KCL)

### HELICOVAXOR

**Development of an oral Helicobacter Pylori vaccine**

Belgium, Czech Republic, France, Switzerland, United Kingdom (ICL)

## Selected R&D projects - international

### UNIVAC

**A „Universal“ influenza vaccine though synthetic,  
dendritic cell-targeted, self-replicating RNA Vaccines**  
Czech Republic, France, Germany, Norway, Russia, UK, Switzerland

### MuleVaClin

**Clinical studies on a multivalent vaccine for human visceral  
leishmaniasis**  
Czech Republic, Italy, Spain, Switzerland





## R&D projects - national

### ODDC

#### Original Drug Development Center

IOCB AS CR, ICT, IEM AS CR, Institut of Physiology AS CR, Apigenex s.r.o., MediTox s.r.o., Quinta-Analytica s.r.o.

### BIOMEDTEST

#### Biomedical models of traumatic spinal cord injury and neurodegenerative diseases in miniature pigs for testing of new therapeutic approaches

Institut of Animal Physiology & Genetics AS CR, MediTox s.r.o.



## Collaboration within professional associations

**CzechBio**

**Association of Czech biotech companies**

**MedChemBio**

**Cluster of medicinal chemistry and chemical biology**





## Contract-based experimental services

### Genetic toxicology & cytotoxicity

*in vitro* (bacteria, mamalian cells), *in vivo* (rodents)

### General toxicology

(acute, sub-chronic, chronic)

rodents, non-rodents

### Safety Pharmacology (CVS, CNS)

dogs, rats

### Immunogenicity/Immunotoxicity

rodents, non-rodents

**Local effects** (irritability, sensitization, implantation, local tolerance)

*in vitro*, rodents, non-rodents

### Non-clinical evaluation

- anticancer pharmaceuticals
- vaccines
- biotech-derived products
- fixed combinations

rodents, non-rodents

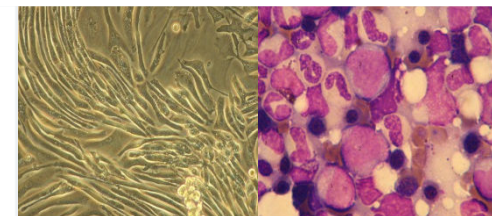
### PK/TK, BA, BEQ studies

rodents, non-rodents

### Biocompatibility of medical devices

rodents, non-rodents





## Contract-based experimental services

### Toxicity to reproduction

Rodents

Screening reproduction toxicity

Prenatal developmental toxicity

One- and two-generation toxicity

Combined reproduction/toxicity studies

Extended one-generation toxicity

### Carcinogenicity

Rodents

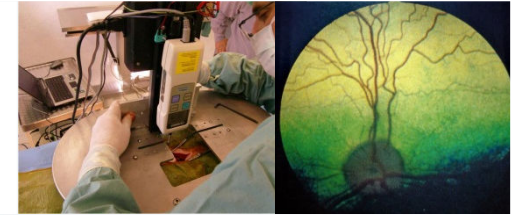
Carcinogenicity (including DRF)

Combined toxicity/carcinogenicity studies

### Biodistribution studies

Rodents, non-rodents

Non-radiolabeled compounds



## Animal models of selected human diseases

**Diabetes** (type II - non-human primates)

**Chronic glaucoma** (dogs)

**Experimental myocardial infarct** (dogs, mini pigs)

**Chronic traumatic spinal cord injury** (mini pigs)

**Acute contact dermatitis** (mini pigs)

**Influenza model** (ferrets)

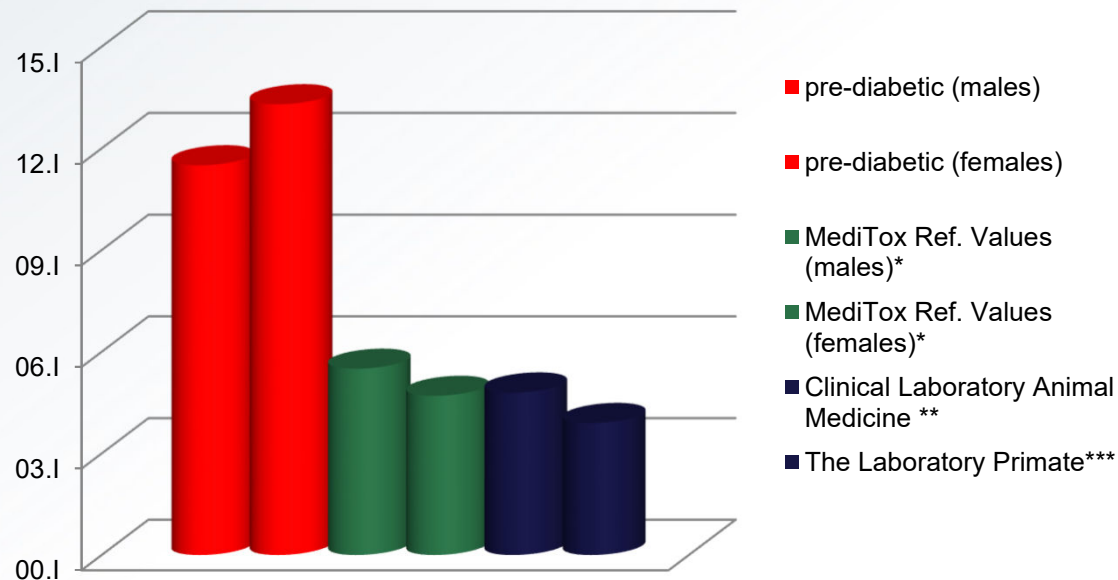
**Osteoarthritis** (guinea pigs, rabbits)





## Experimental model of diabetes, rhesus monkeys

- Most common in older, obese animals
- Period of obesity-associated insulin resistance initially with compensatory insulin secretion
- Pathological changes in pancreatic islets similar to those seen in human
- Changes in plasma lipid and lipoprotein concentrations and lipoprotein composition



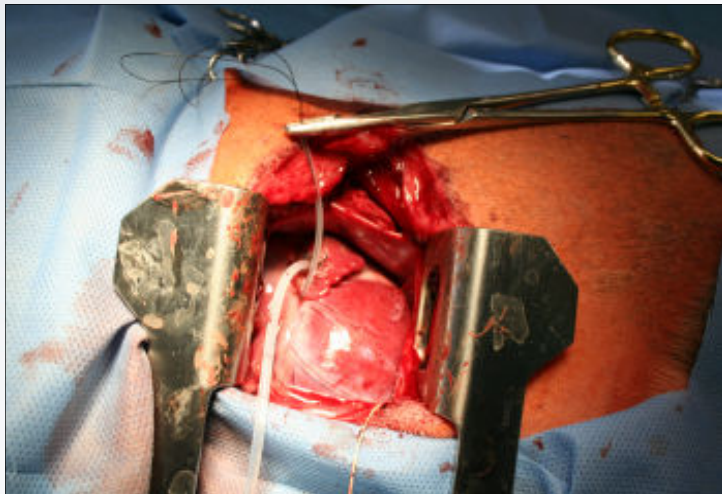




## Experimental model of myocardial infarction, dog

- Left ventricular dysfunction induced by by ligation of the left coronary artery (myocardial ischemia) followed by heart reperfusion.
- Morphometric analysis of area at risk and area of infarction performed using Coomassie blue

*Arteria coronaria* occlusion  
90-minute ischemia following 5-hour re-perfusion

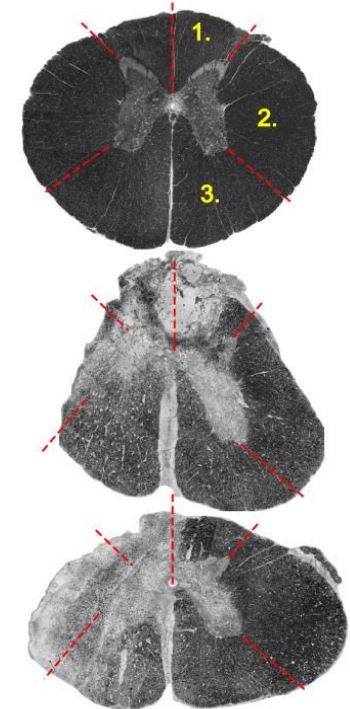
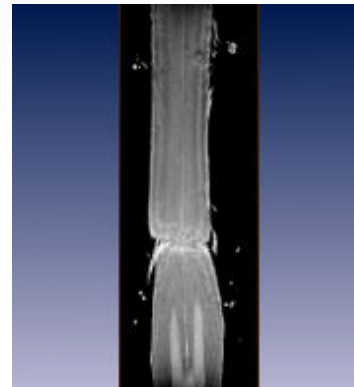
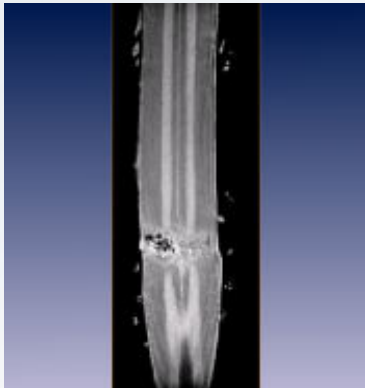


Myocardial section (Coomassie blue injected into *arteria coronaria*):  
Dark blue – intact myocardium  
Red – ischemia zone  
White - infarctation zone



## Chronic traumatic spinal cord injury model, pig

- Computer-managed device providing **strictly repeatable spinal cord injury**, either in the **thoracic** or **lumbal** region
- All essential reflexes (feeding, urination and defecation) preserved
- Long lasting survival of paraplegic animals





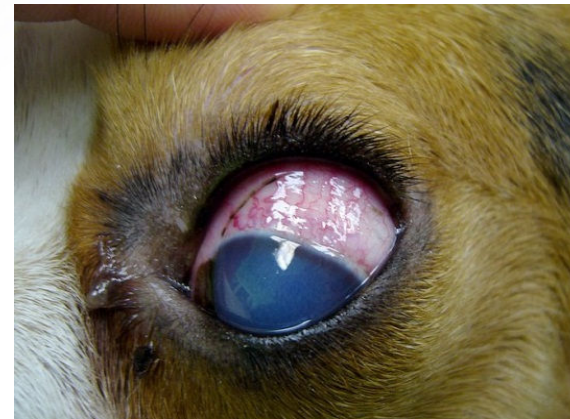
## Experimental chronic glaucoma, dogs

*„More than 70 million people worldwide suffer from glaucoma. Glaucoma is leading cause of blindness.“*

**Induced by intraocular injection of chymotripsine**

**Revealing characteristic clinical signs**

- elevation of IOP
- corneal opacity
- dilated episcleral blood vessels at the corneal edge
- reduced or absent pupillary reflex
- uveitis.





## Ferret model for safety and efficacy of influenza therapy

Ferrets (*Mustela putoria*) emulate numerous clinical features associated with human disease; this is especially the case with regard to influenza

**Clinical and clinical laboratory features shared by humans and ferret model following virus infection**

- Fever
- Nasal secretion
- Coughing
- Serum abnormalities
- Weight loss and/or anorexia
- Lethargy
- Lymphopenia
- Transmission to susceptible contacts
- Hypercytokinemia
- Distribution of sialic acid in respiratory tract



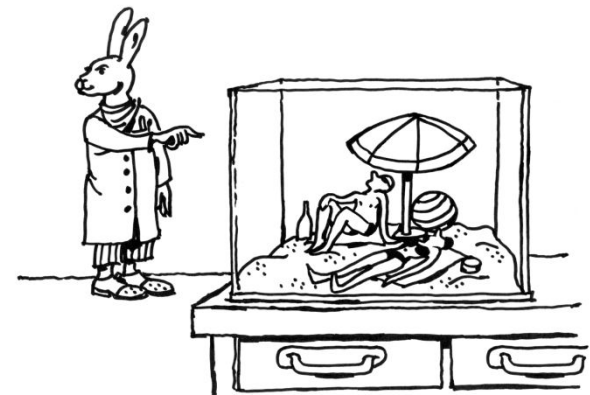


## Breeding of laboratory animals

### Non-rodents

Rhesus macaques (*Macaca mulatta*, monitored quality)

Beagle dogs (monitored quality)



## References

**Amega Biotech**, Argentina

**Bharat Biotech**, India

**Bio-Assistance**, Canada

**Bioxodes**, France

**California Univ**, USA

**Celon Pharma**, Poland

**CONTIPRO a.s.**, CR

**CRONET-Sagl**, Switzerland

**DECHRA Veterinary Products**, UK

**DelSiTech Ltd.**, Finland

**EMS**, Brazil

**Evestra**, Germany

**Faraday, Inc.**, USAFATRO, Italy

**Fusion Pharma**, Russia

**Gelesis Inc.**, USA

**IOCB CAS**, CZ

**KRKA**, Slovenia

**Lesaffre**, France

**Mabion**, Poland

**Medicine Development**, Australia

**NovoNordisk**, Denmark

**Oxford University**, UK

**Rottapharm**, Italy

**Sanofi Group** (Zentiva)

**Sunpharma**, India

**Univ Hospital Basel**, Switzerland

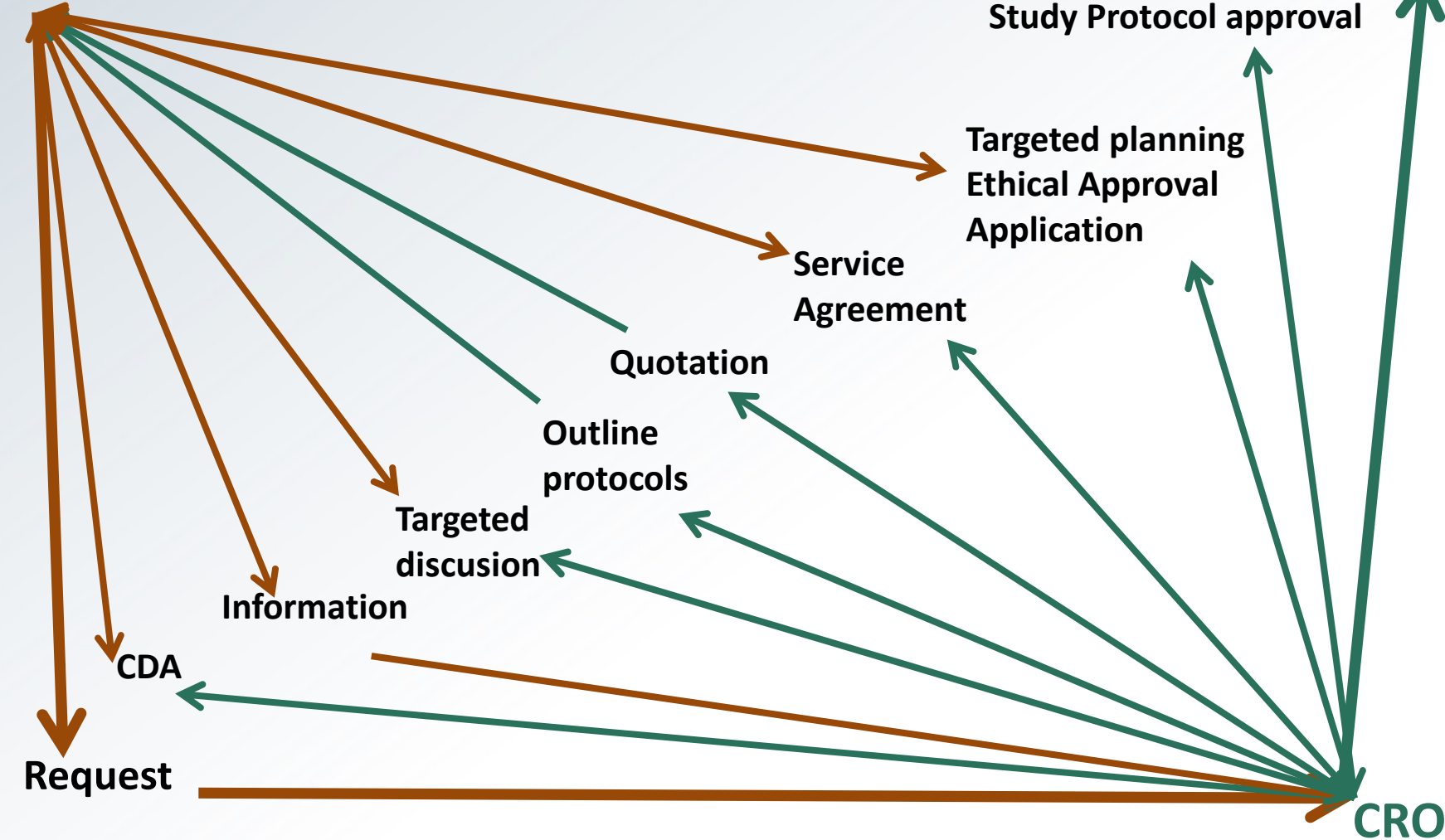
**Triveritas**, USA/UK

**Vetcare Oy**, Finland

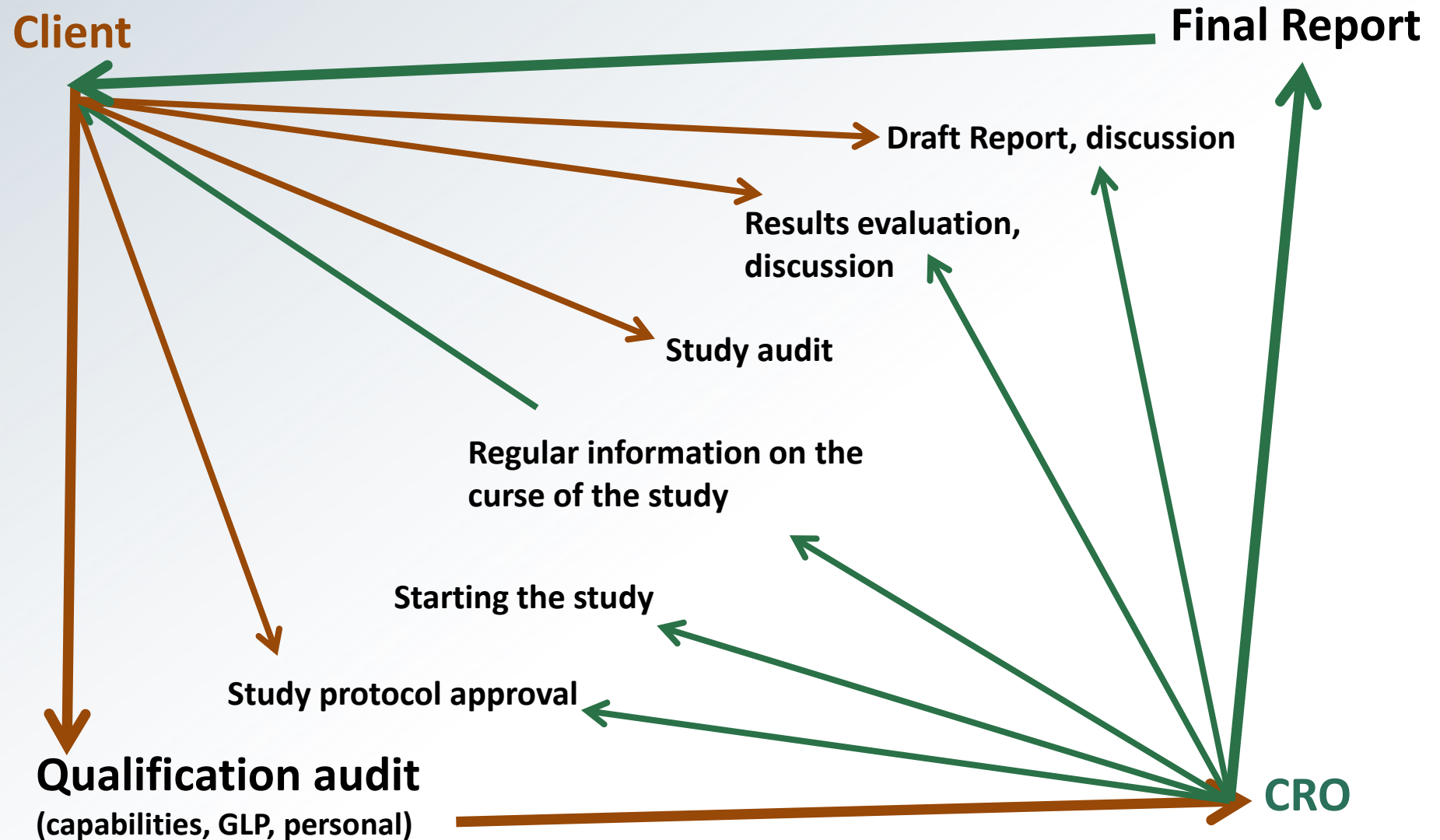
## Communication chart

## Start of the study

Client



## Sequence of events during the project





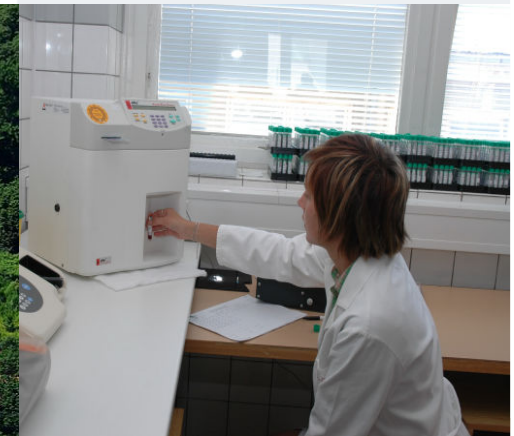
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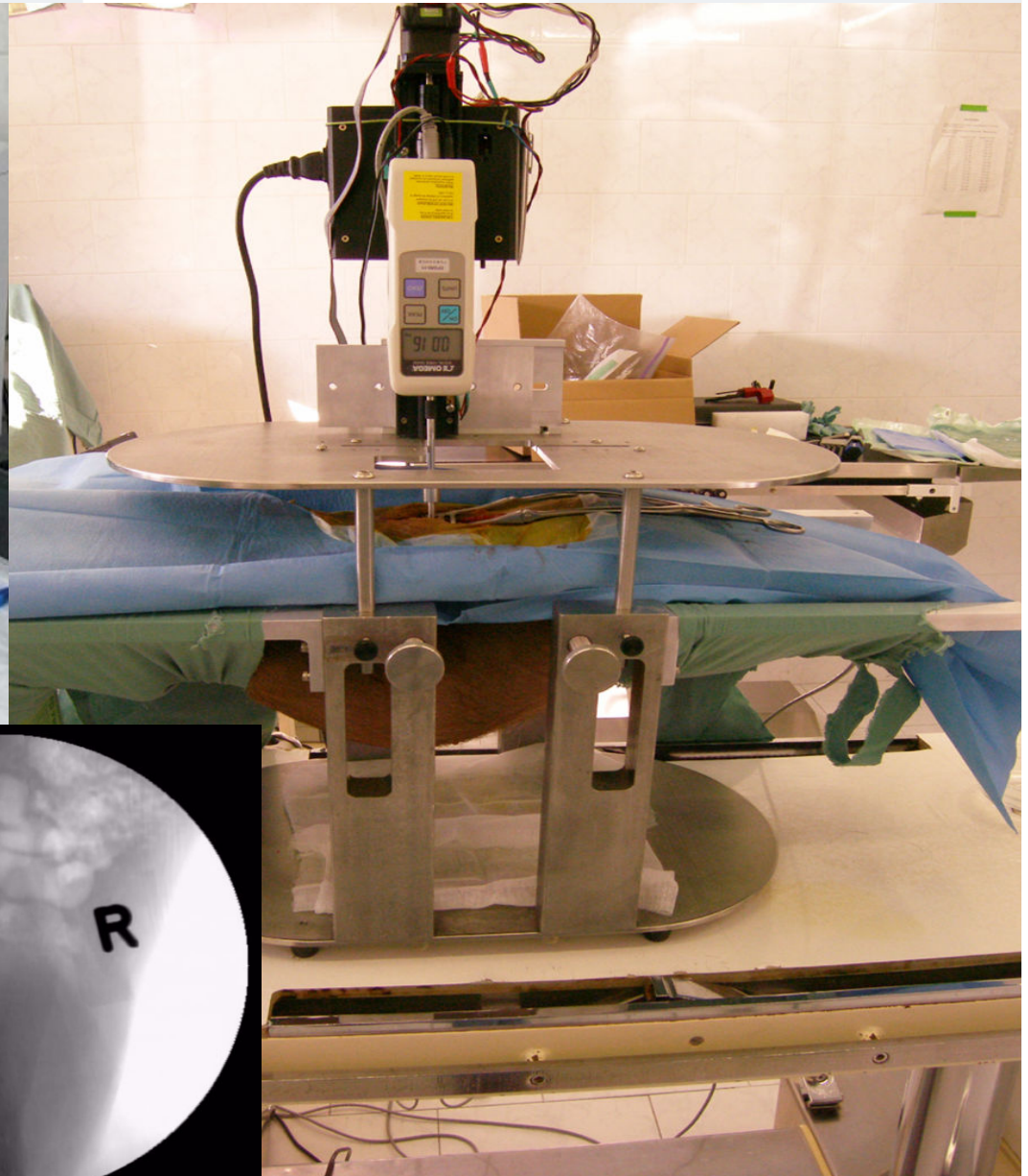
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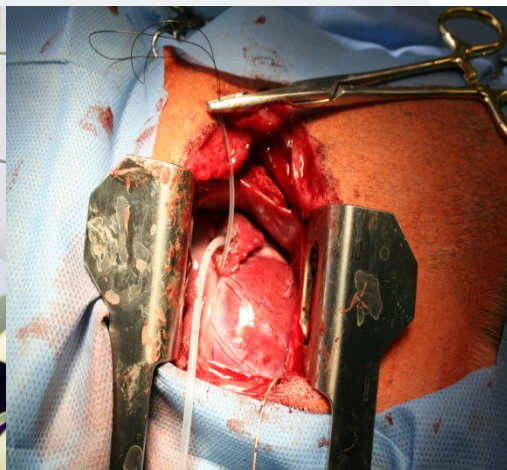
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