

GLP Certificate holder

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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

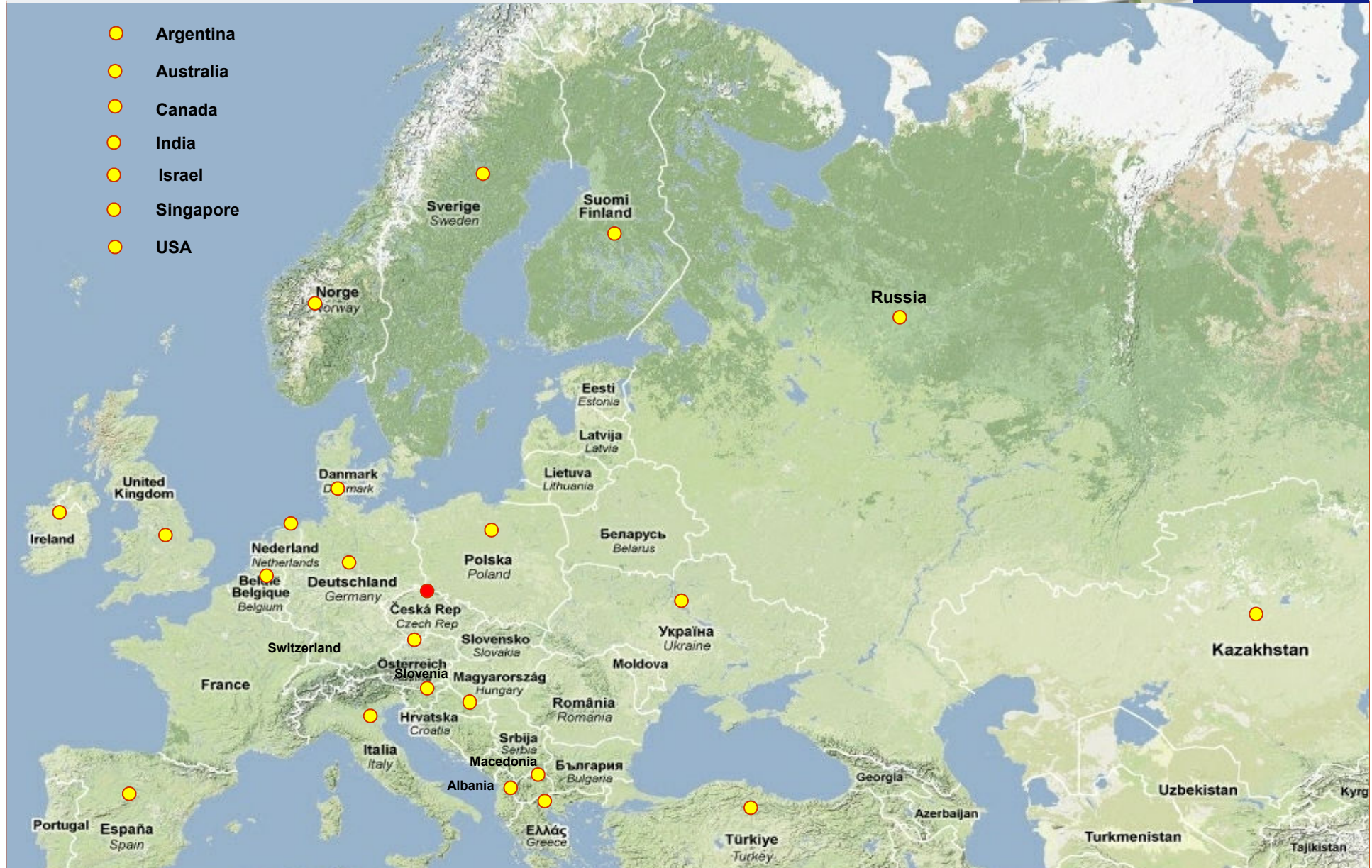


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- Argentina
- Australia
- Canada
- India
- Israel
- Singapore
- USA





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

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, arthrosis

Laboratory animal breeding

Non-human primates, dogs, rodents

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

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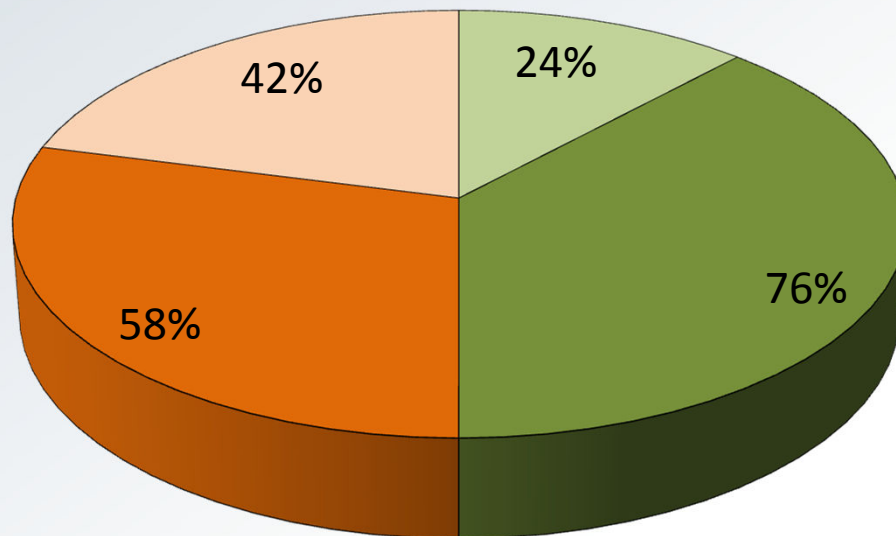
Approval for handling with GMO in compliance with Act

No. 153/2000 Coll.



Summary information

Structure of experimental work



■ R&D activities

■ Contract-based activities

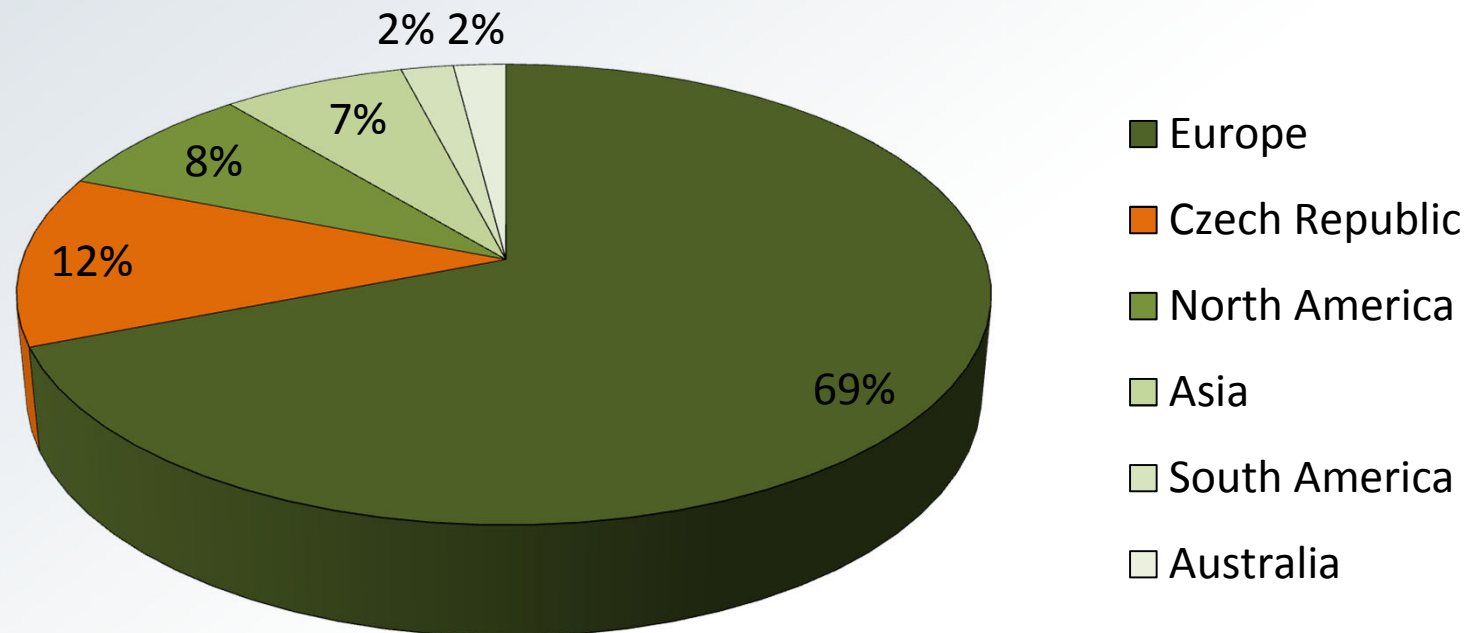
■ GLP-compliant

■ Non-GLP



Summary information

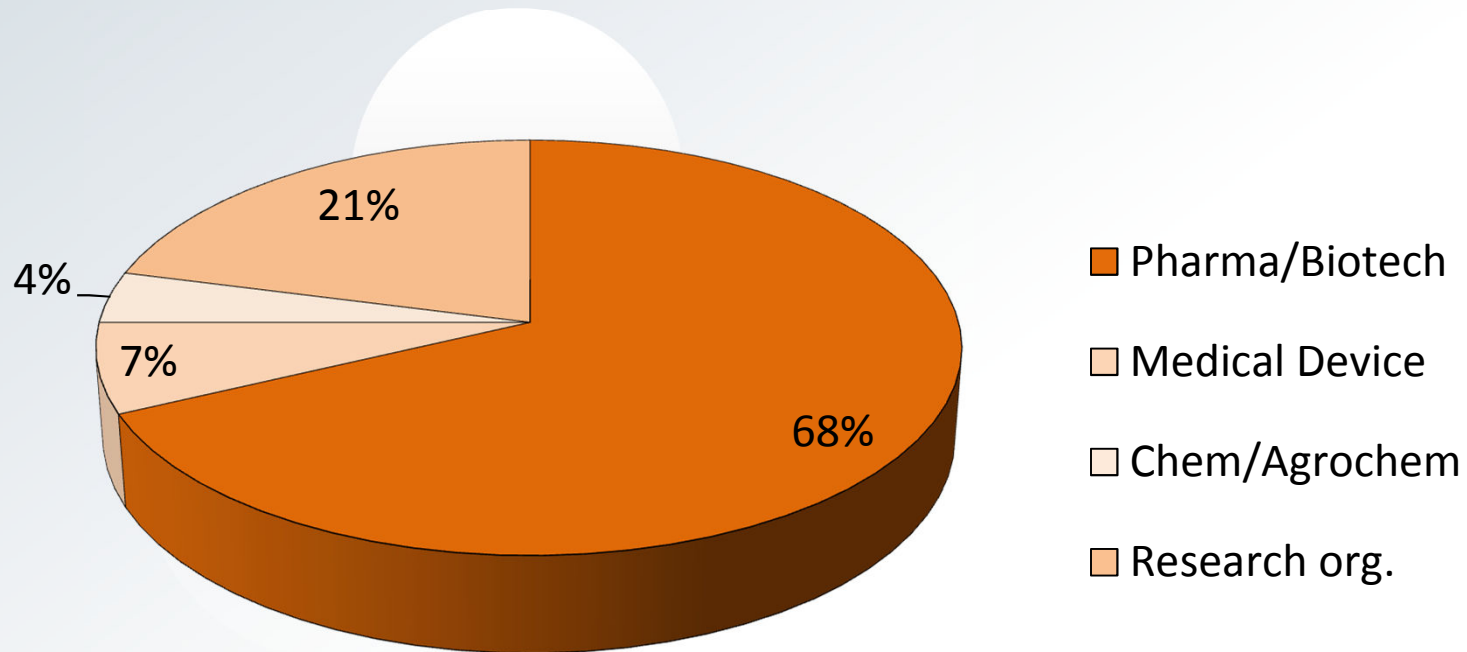
Structure of clients





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

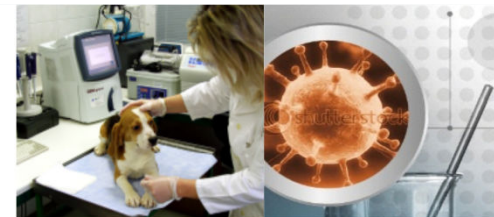
CzechBio

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

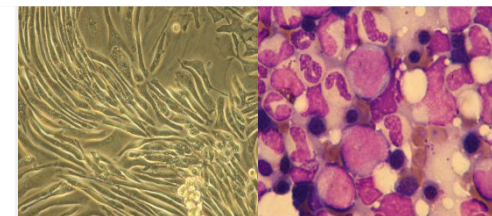
PK/TK, BA, BEQ studies

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

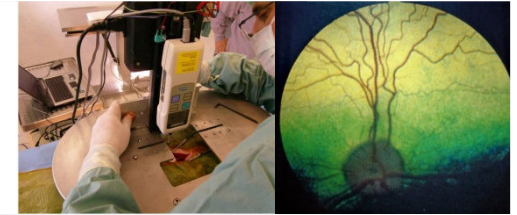
Carcinogenicity (including DRF)

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)

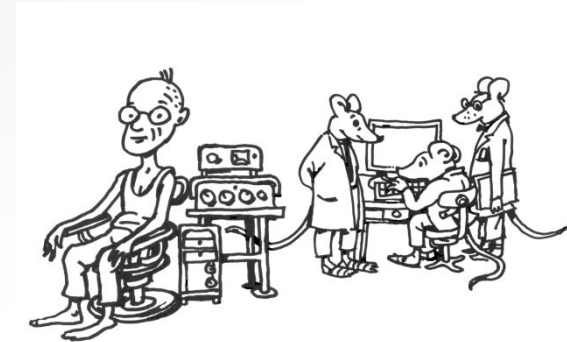
Experimental myocardial infarct (dogs, mini pigs)

Chronic traumatic spinal cord injury (mini pigs)

Acute contact dermatitis (mini pigs)

Influenza model (ferrets)

Osteoarthritis (guinea pigs, rabbits)



Models under development

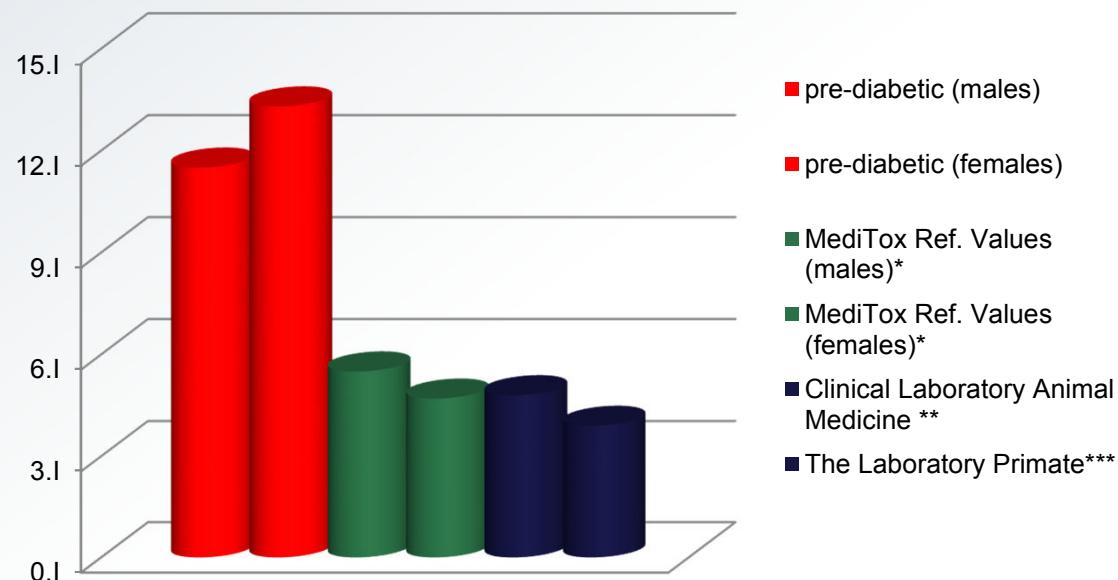
Diabetes (dogs, mini pigs)

Enterocolitis (rats)



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

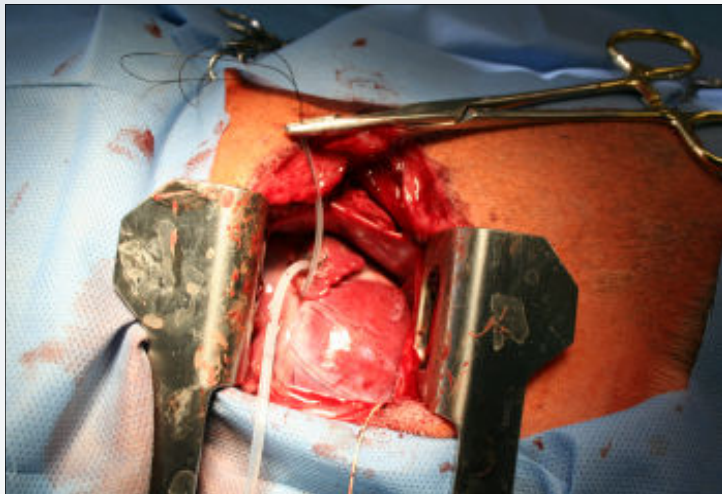




Experimental model of myocardial infarction, dog

- 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

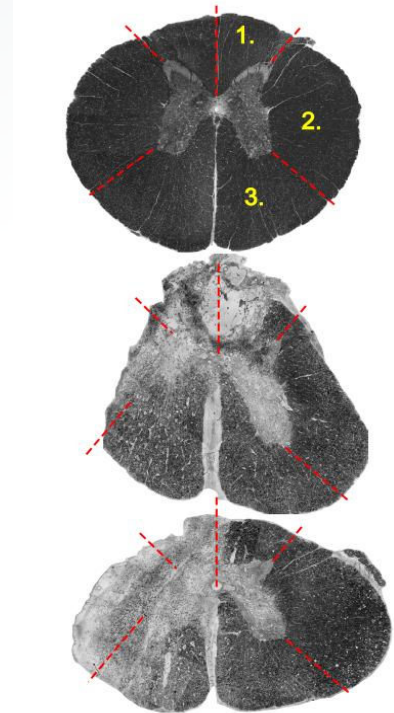
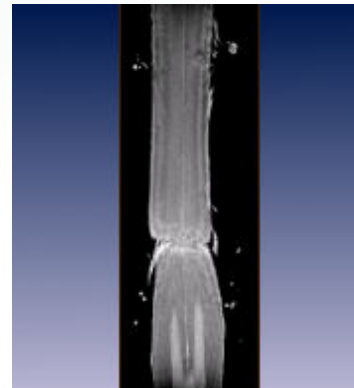
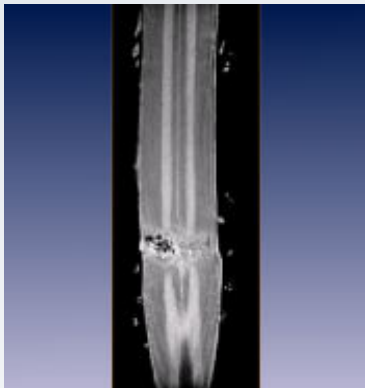


Myocardial section (Coomassie blue injected into *arteria coronaria*):
Dark blue – intact myocardium
Red – ischemia zone
White - infarctation zone



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





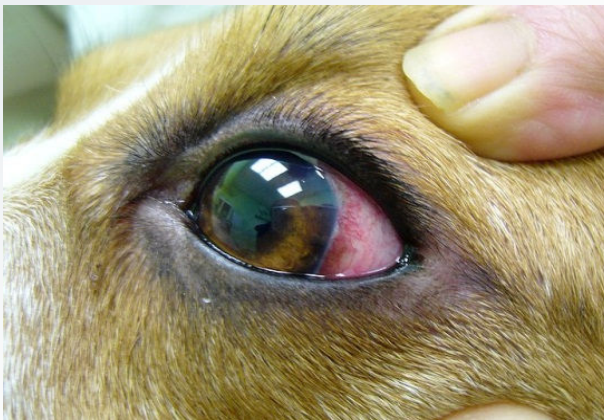
Experimental chronic glaucoma, dogs

„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

Rodents

Rats (Wistar:Han, SPF quality)

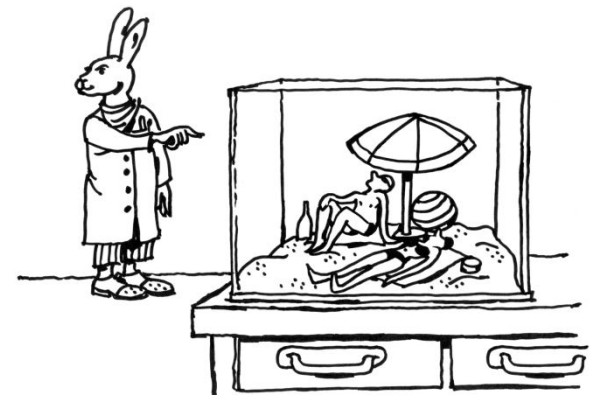
Mice (NMRI, SPF quality)

Guinea pigs (*Cavia aperea f. porcellus*, monitored quality)

Non-rodents

Rhesus macaques (*Macaca mulatta*, monitored quality)

Beagle dogs (monitored quality)



References

AGINKO AG, Switzerland

Amega Biotech, Argentina

AmVac, Germany

Baxter Biosciences, Austria

Bio-Assistance, Canada

Contipro a.s., Czech Republic

Dechra Veterinary Products, UK

Fusion Pharm, Russia

Gelesis Inc., USA

IOCB, Czech Republic

KRKA, Slovenia

Lesaffre, France

Lupin Pharma, India

Mabion, Poland

Max-Planck Inst. of Inf. Biol. Germany

Midatech, UK

NovoNordisk, Denmark

OCT Clinical Trials, USA

Oncos Therapeutics, Finland

Oxford University, UK

Pharmathen, Greece

Sanofi Group (Zentiva)

Sigmoid Pharma, UK

Sun Pharmaceuticals, India

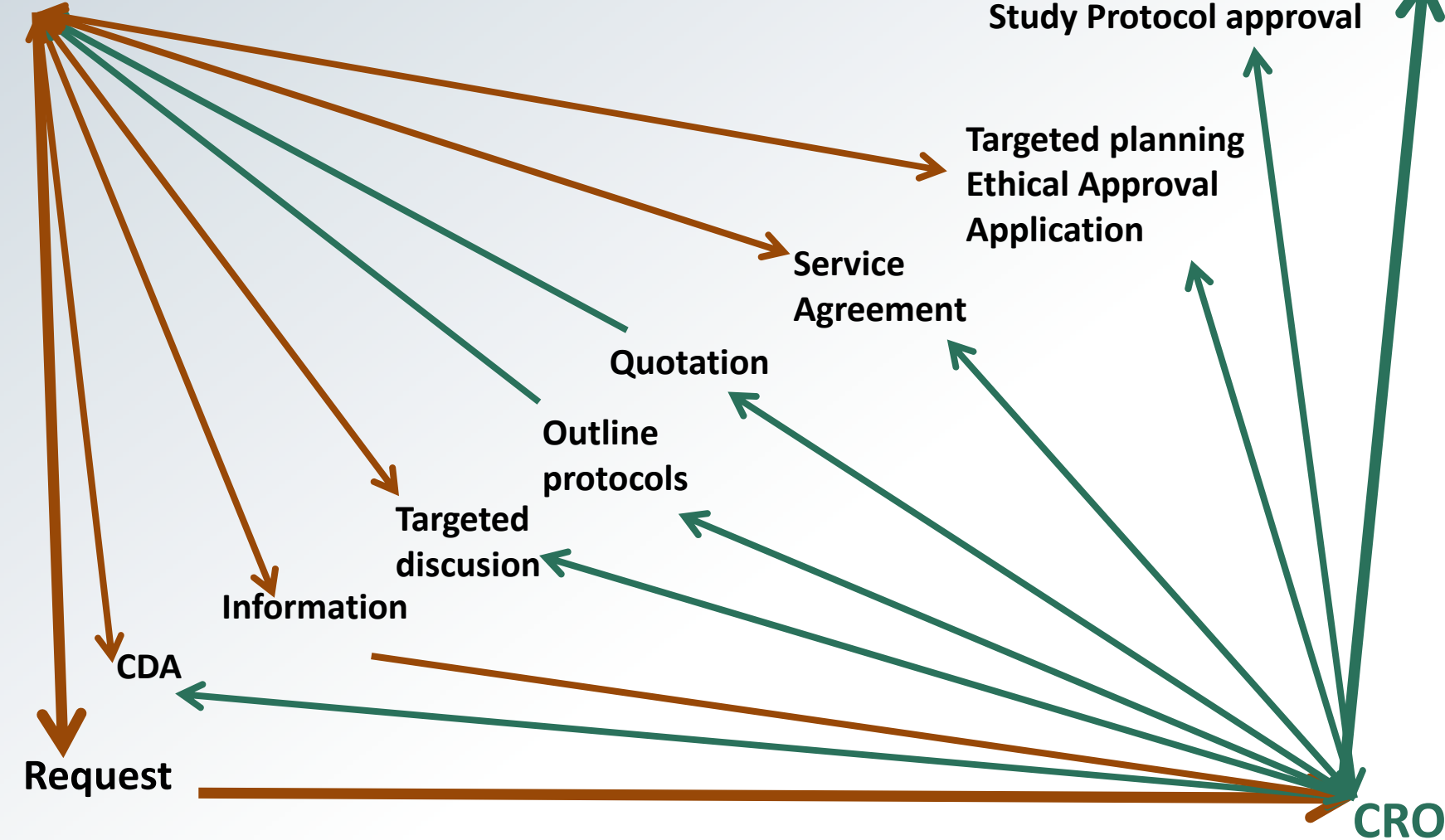
Triveritas, USA/UK

Vetcare Oy, Finland and more...

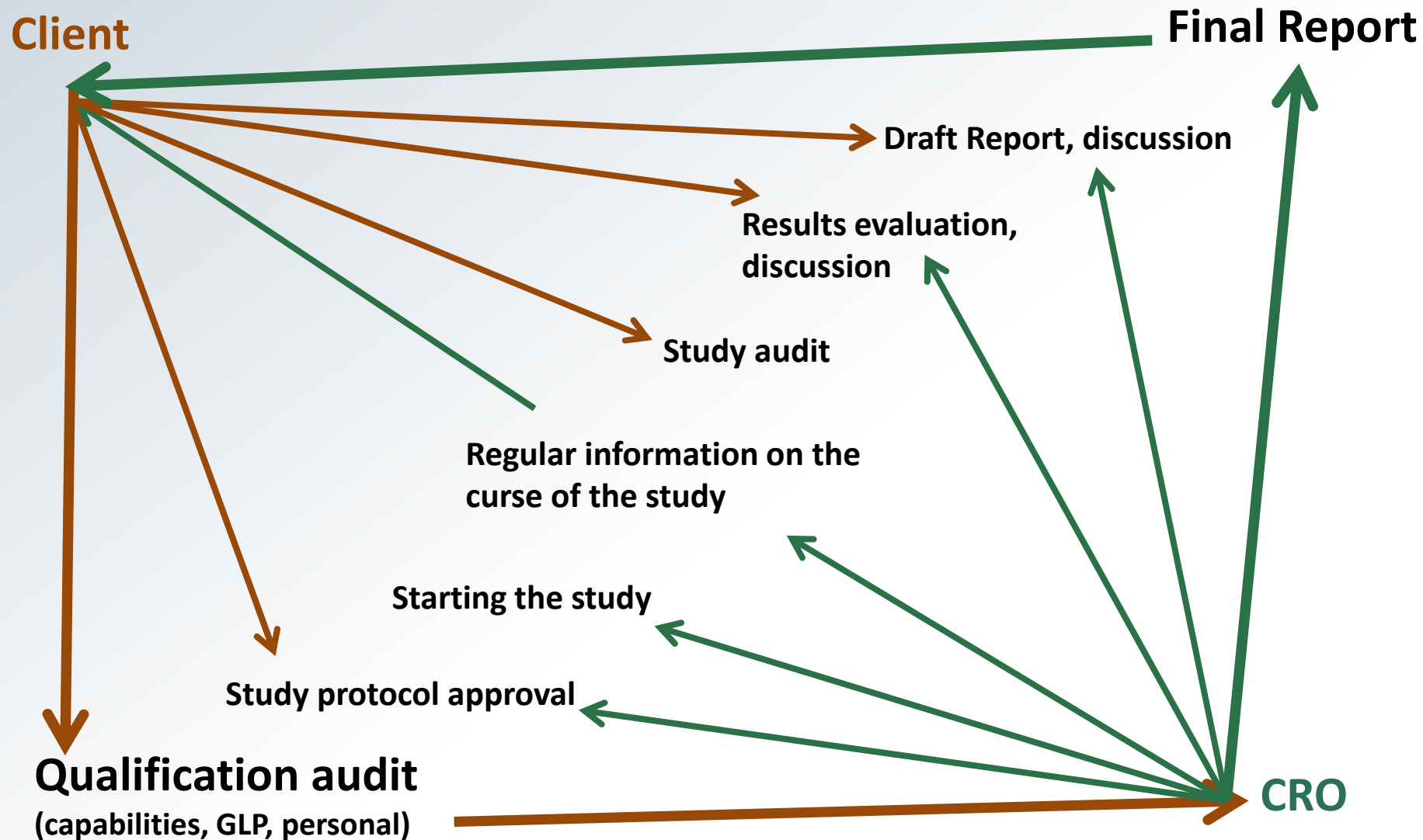
Communication chart

Start of the study

Client

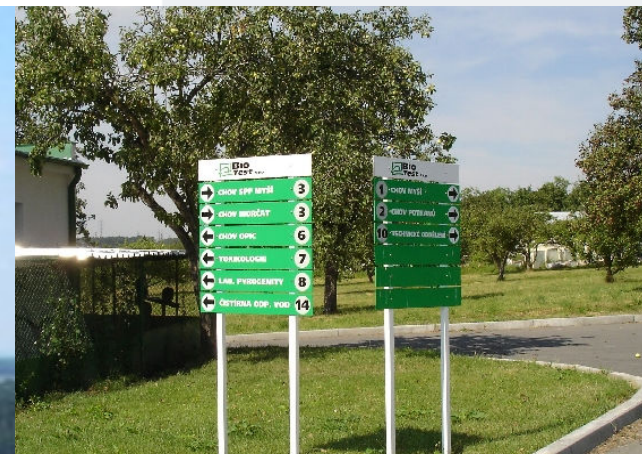


Sequence of events during the project



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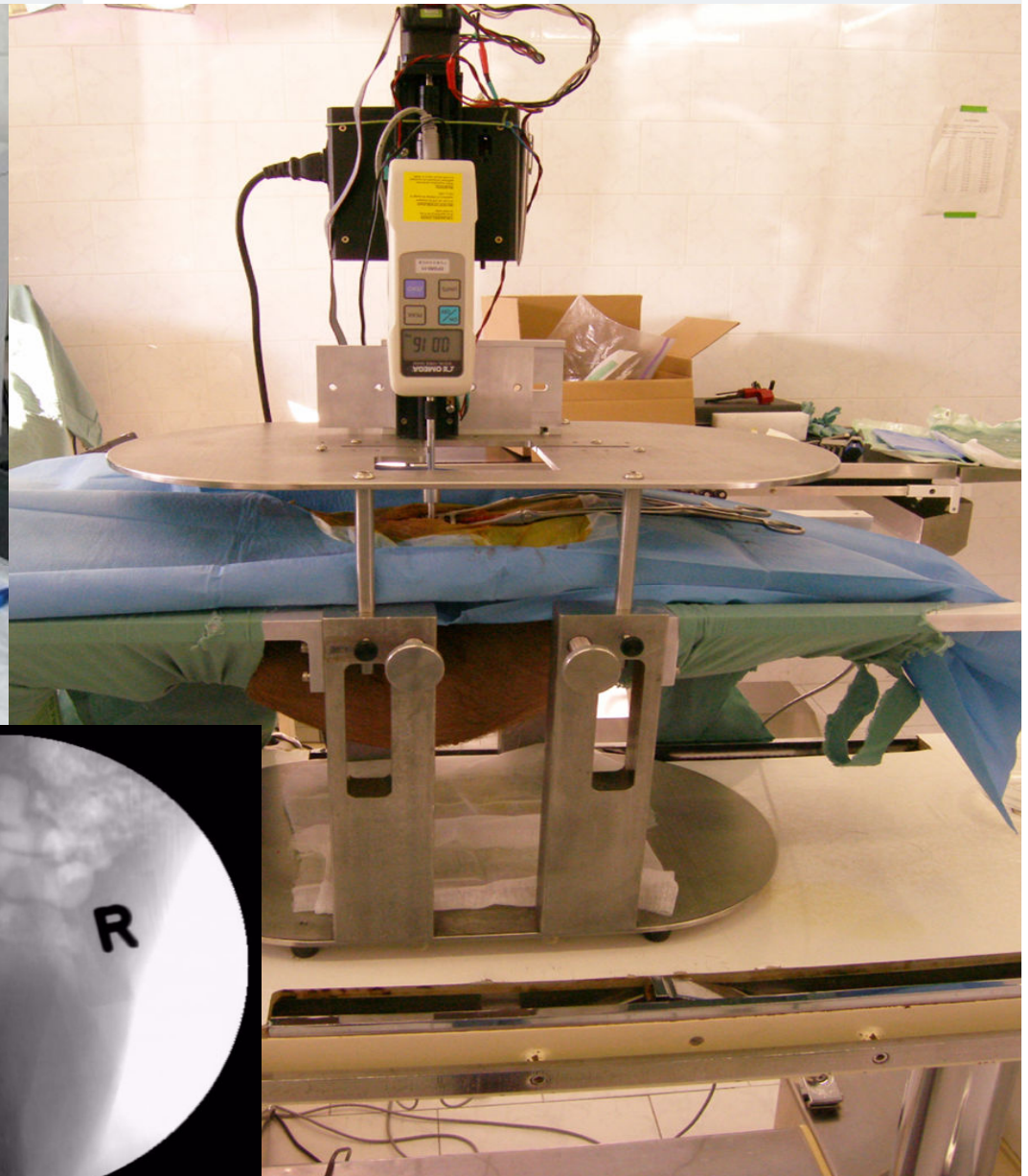
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since April 2013 new name of


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