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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

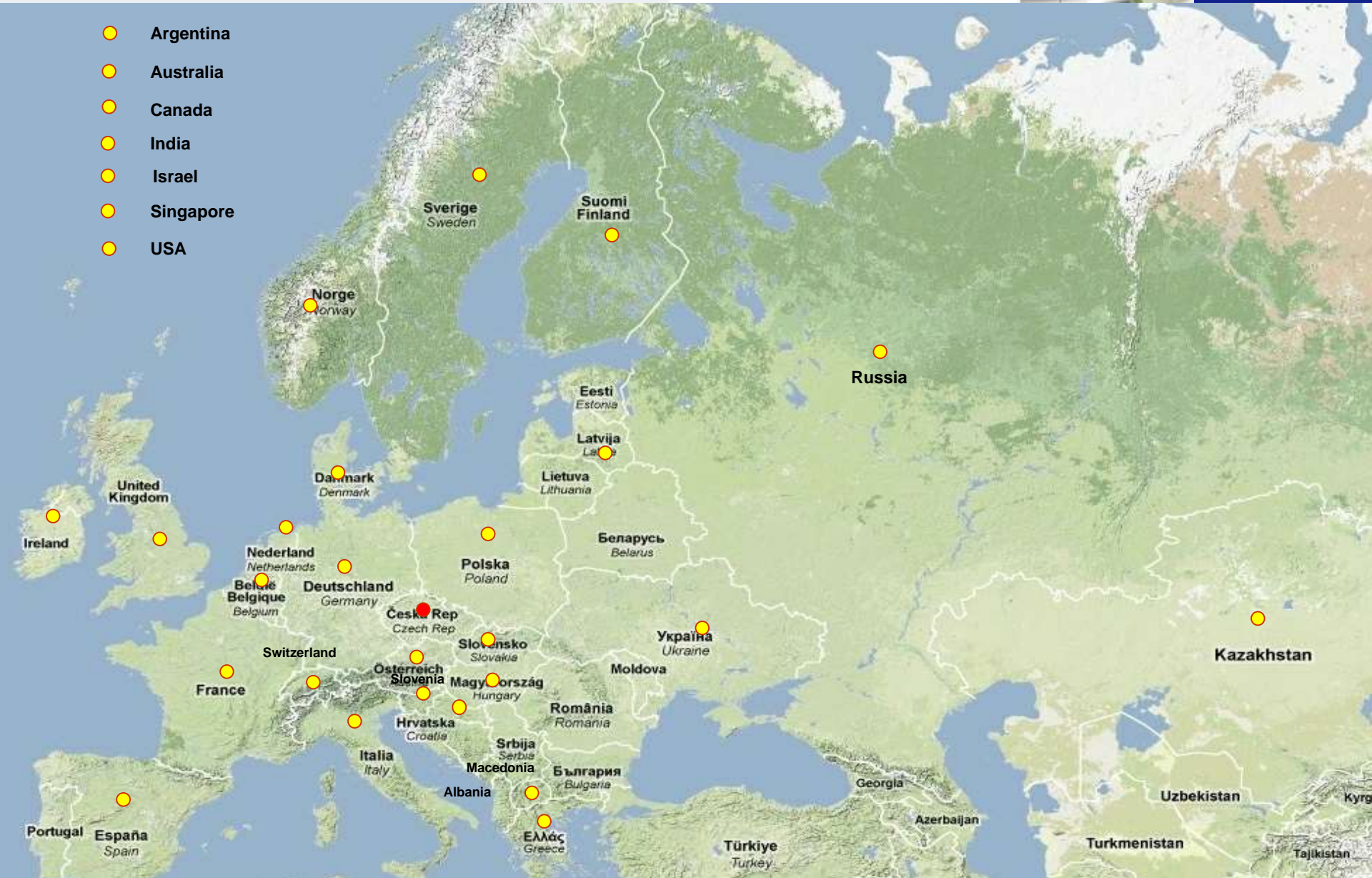


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per aspera ad astra



- 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

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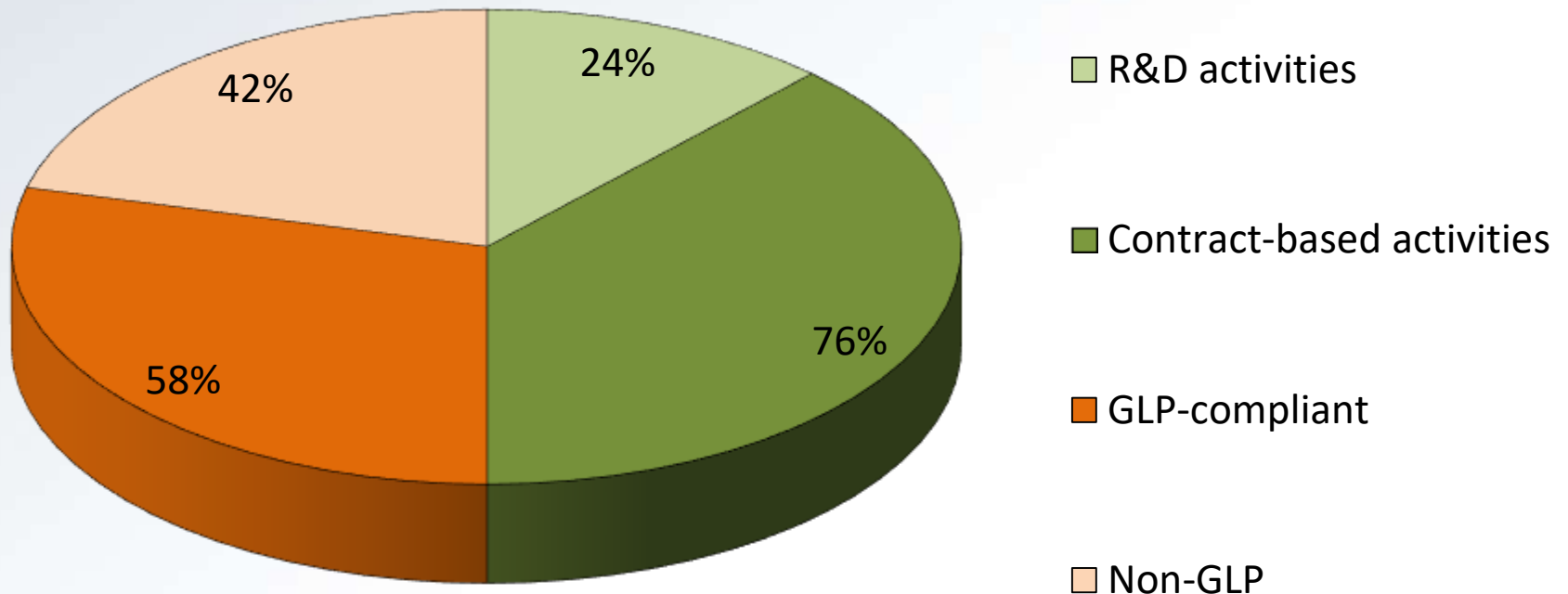
Approval for handling with GMO in compliance with Act

No. 153/2000 Coll.



Summary information

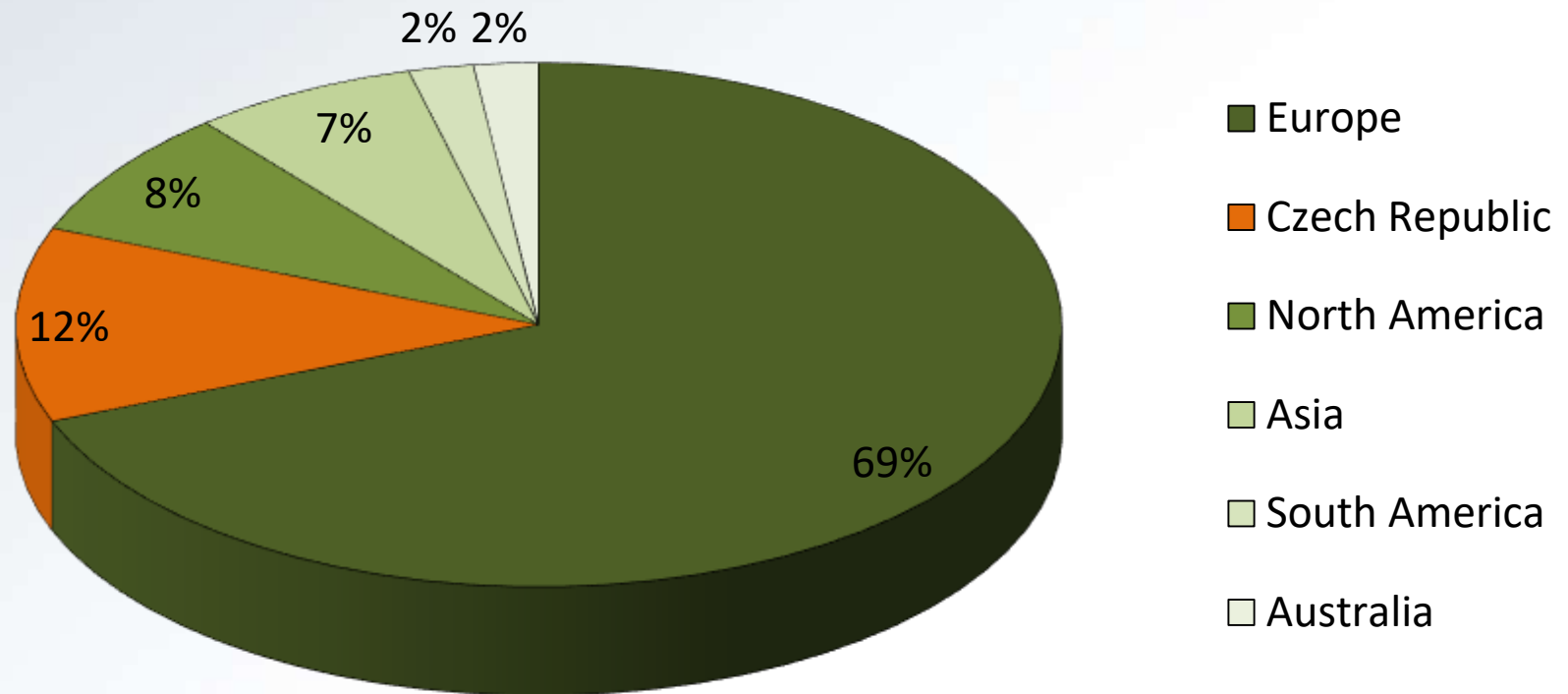
Structure of experimental work





Summary information

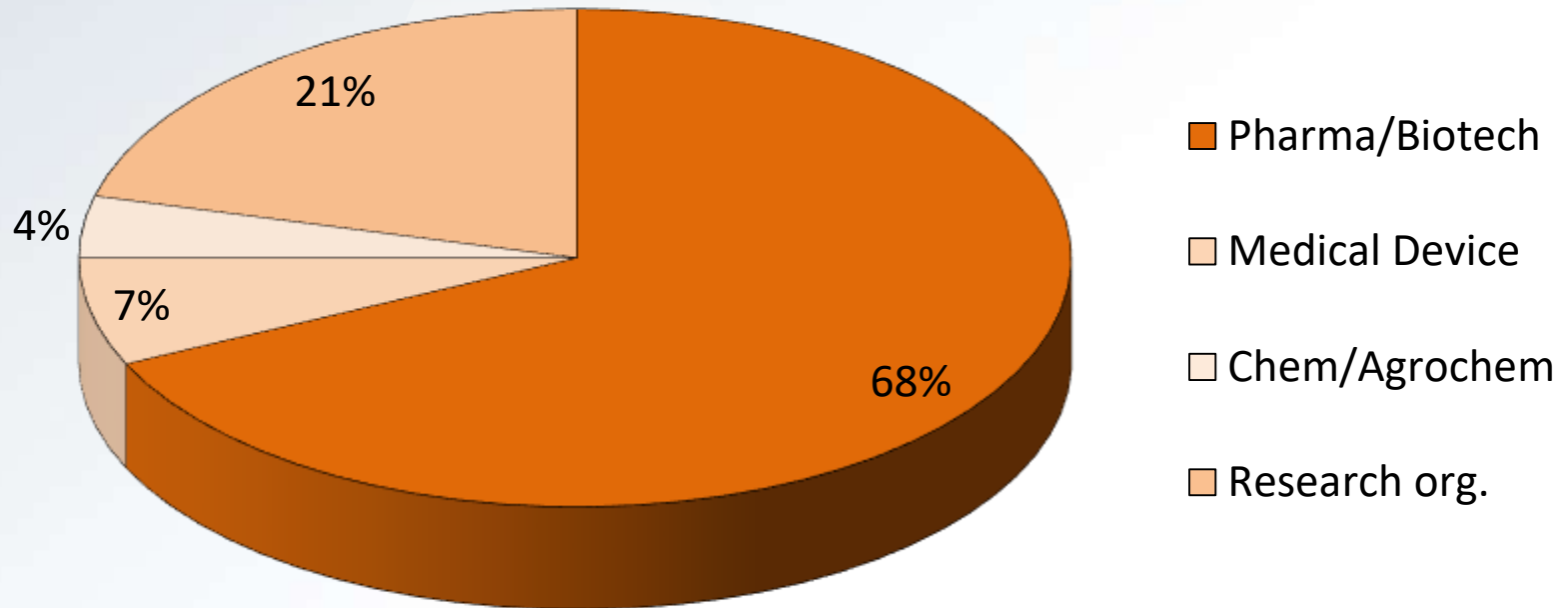
Structure of clients





Summary information

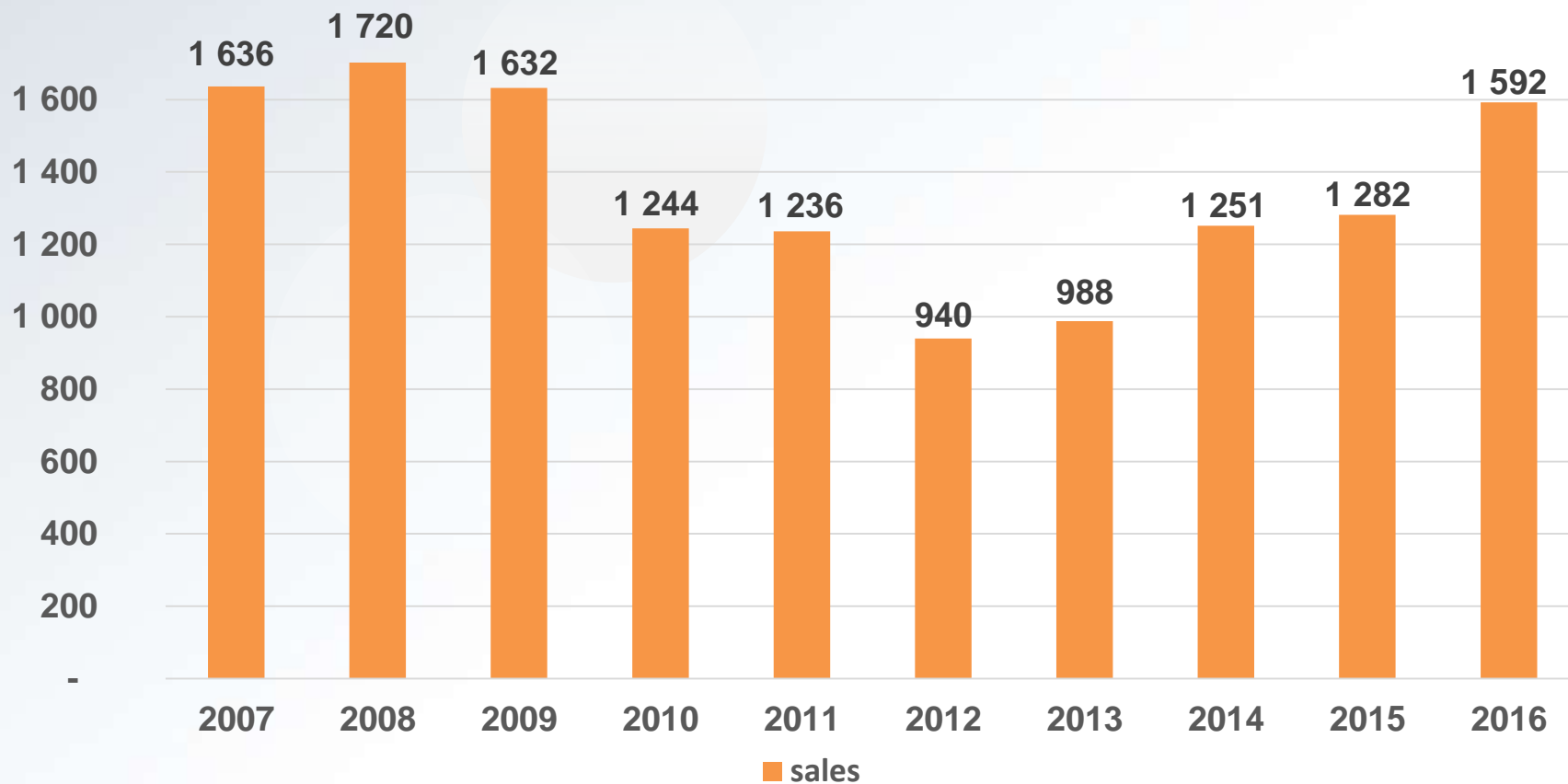
Structure of clients





Summary information

Company sales in EUR (thousands)





Investments

During 2016 – 2017 MediTox invests 600 000 EUR in development of its facilities.

- reconstruction of housing for NHP, dogs, rabbits, ferrets, guinea pigs
- widening of experimental capacities for dogs
- widening capacities for dog breeding





Selected R&D projects

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)

MuleVaClin

Clinical studies on a multivalent vaccine for human visceral leishmaniasis

Czech Republic, Italy, Spain, Switzerland



National R&D projects

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.





Contract-based experimental services

Study type	Guideline	Test system
Genetic toxicology & cytotoxicity	ICH, OECD, FDA, ISO 10993	<i>In vitro, in vivo</i> (rodents)
General toxicology (acute, sub-chronic, chronic)	ICH, OECD, FDA	Rodents, non-rodents
Safety Pharmacology (CNS, CVS)	ICH, FDA	Rats, dogs
Local effects (irritability, sensitization, implantation, local tolerance)	ICH, OECD, ISO 10993	Rodents, non-rodents
Non-clinical evaluation (anticancer pharmaceuticals, vaccines, biotech-derived products, fixed combinations, etc.)	ICH	Rodents, non-rodents)
PK, TK, BA, BEQ	ICH, OECD, VICH	Rodents, non.-rodents



Contract-based experimental services

Study type	Guideline	Test system
Target animal safety studies	VICH	Non-rodents
Biocompatibility of medical devices	ISO 10993-1, 2, 3, 5, 6, 10, 11, 12	Rodents, non-rodents
Toxicity to reproduction (Screening reproduction toxicity, Prenatal developmental toxicity, One- and two-generation toxicity, Combined reproduction/toxicity)	ICH, OECD	Rodents
Carcinogenicity (DRF, combined carcinogenicity/toxicity)	ICH, OECD	Rodents
Biodistribution studies (Non-radiolabeled compounds)	ICH, OECD	Rodents



Animal models of selected human diseases

Diabetes (type II - non-human primates)

Chronic glaucoma (dogs)

Experimental myocardial infarct (dogs, mini pigs)

Acute contact dermatitis (pigs)

Influenza model (ferrets)

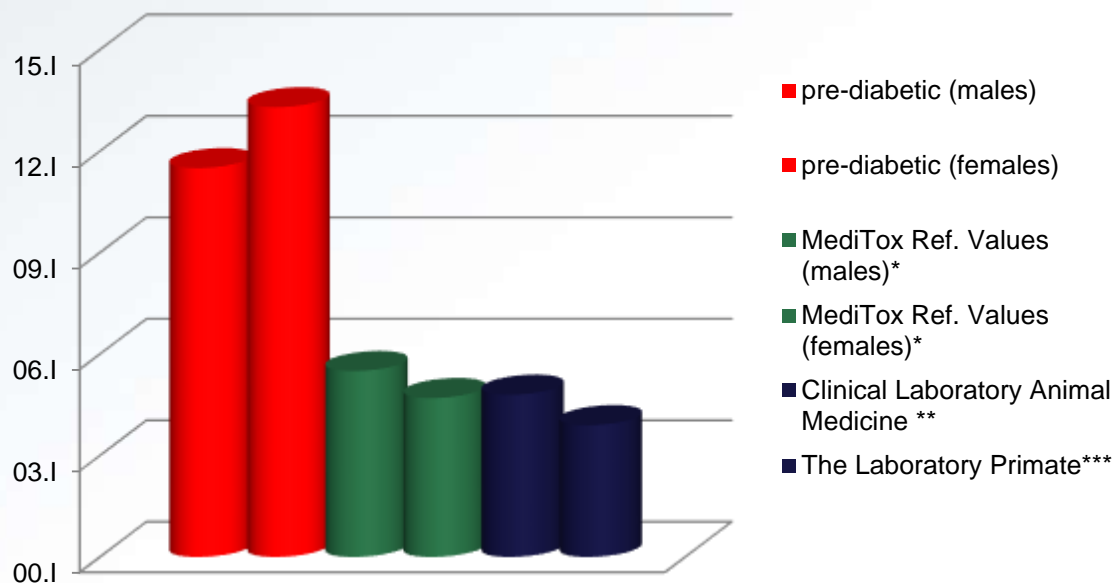
Osteoarthritis (guinea pigs, rabbits)





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





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



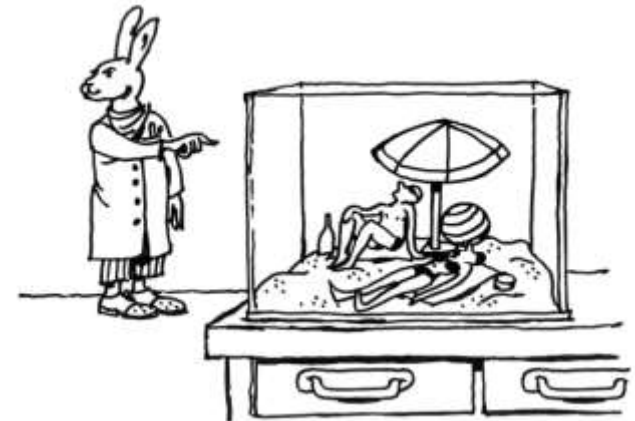


Breeding of laboratory animals

Non-rodents

Rhesus macaques (*Macaca mulatta*, monitored quality)

Beagle dogs (monitored quality)



References

Amega Biotech, Argentina

Bharat Biotech, India

Bio-Assistance, Canada

BIOVET AD, Belgium

California Univ, USA

Celon Pharma, Poland

CONTIPRO a.s., CR

CRONET-Sagl, Switzerland

DelSiTech Ltd., Finland

EMS, Brazil

Evestra, Germany

Faraday, Inc., USA

FATRO, Italy

Gelesis Inc., USA

Immuneed, Sweden

KRKA, Slovenia

Lesaffre, France

Medicine Development, Australia

NovoNordisk, Denmark

Olainfarm, Latvia

Oxford University, UK

Pharmathen, Greece

Rottapharm, Italy

Sanofi Group (Zentiva)

Sunpharma, India

Univ Hospital Basel, Switzerland

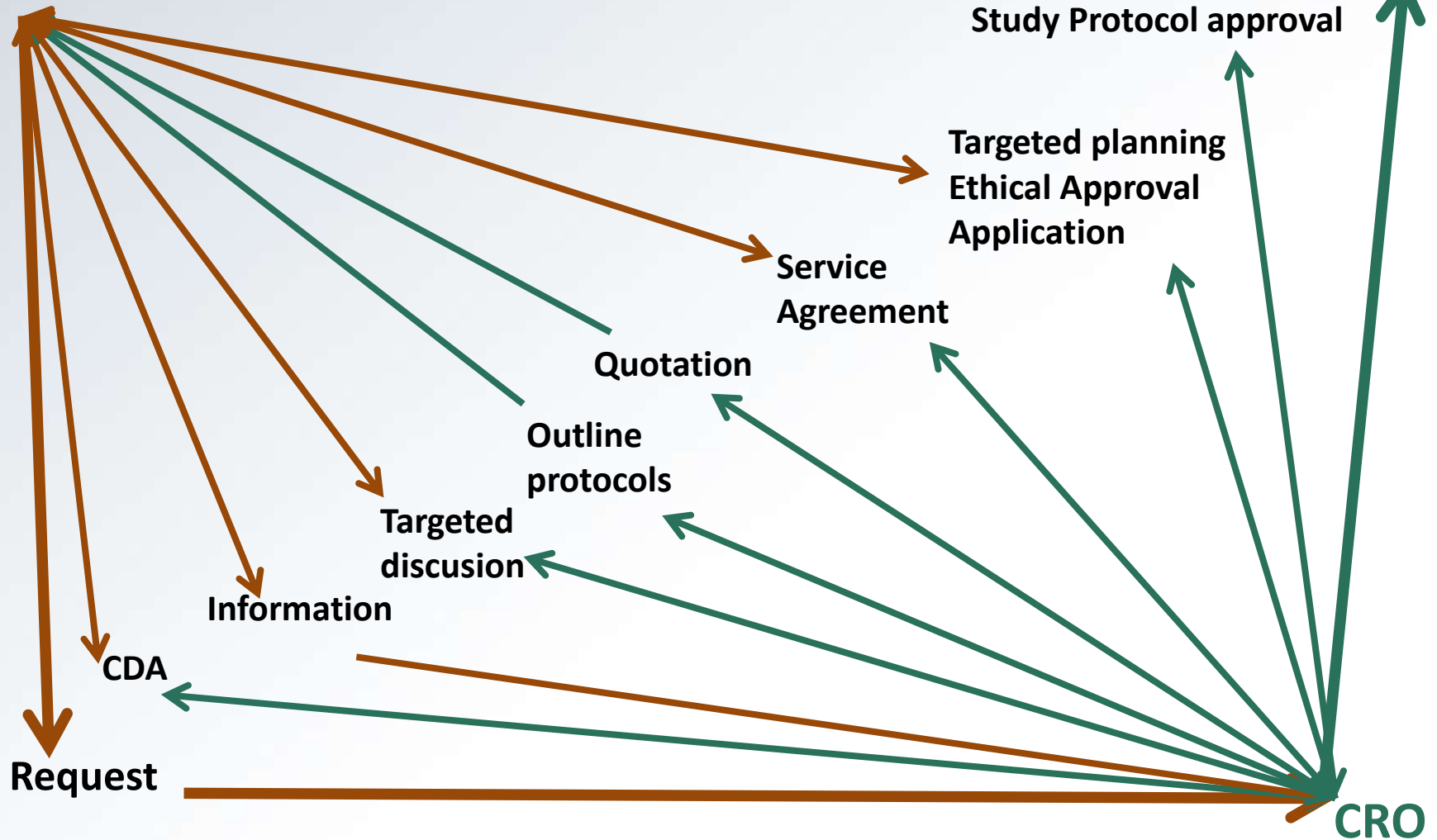
Triveritas, USA/UK

Vetcare Oy, Finland

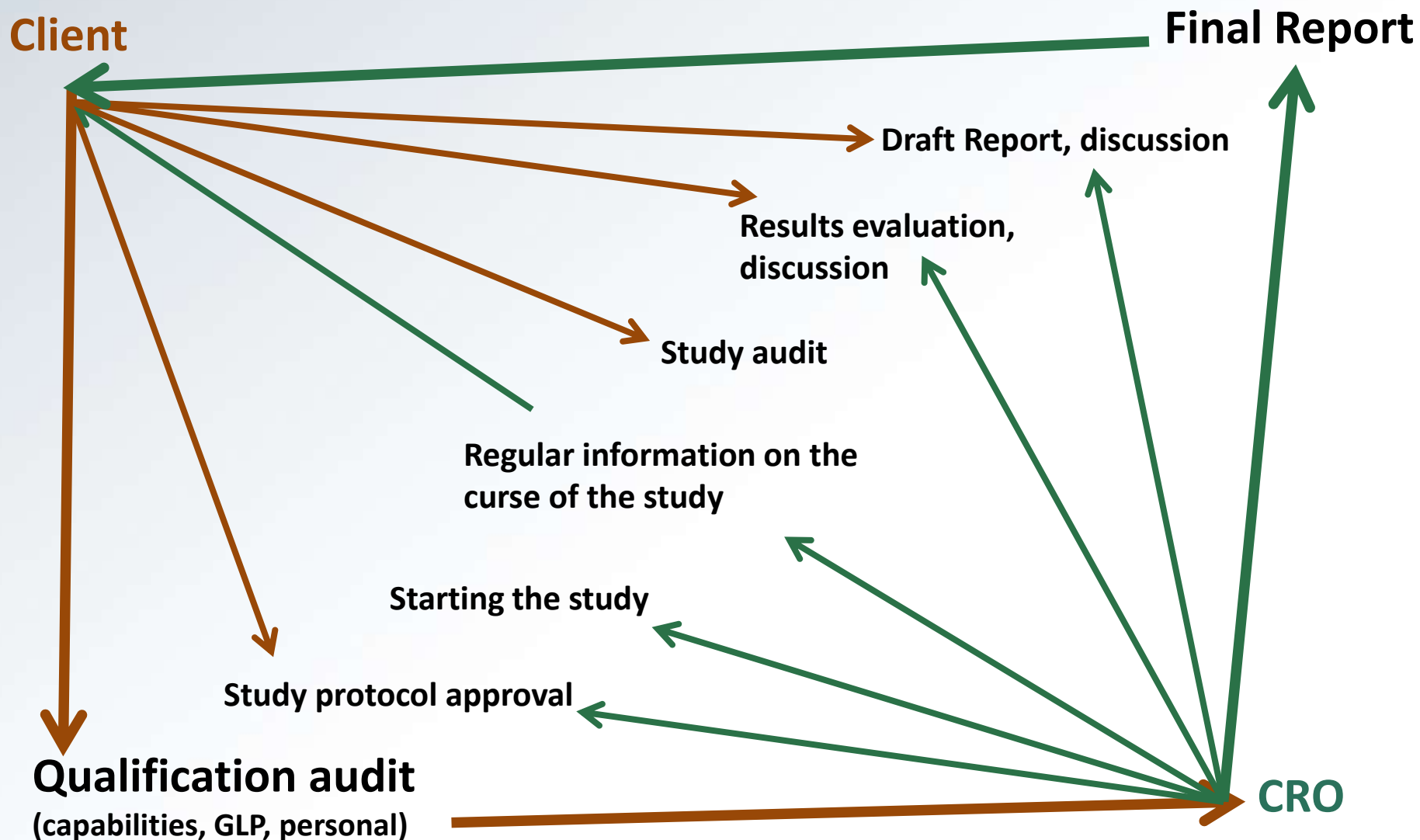
Communication chart

Client

Start of the study



Sequence of events during the project



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GLP Certificate holder

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