



GLP Certificate holder



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Pre-clinical research and development

(CVS disorders, diabetes, anti-flu vaccines, oncology)

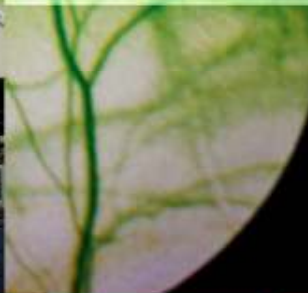
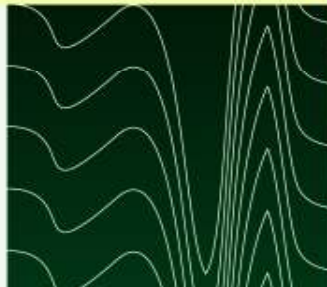
Comprehensive toxicological service

(human and veterinary pharmaceuticals, medical devices)

Customized immunization and antibody production

Accredited breeding facility

(macaques, dogs, ferrets, etc.)



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Huntington's diseases models

Hemodynamic laboratory

Hereditary melanoma model





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History

1951: Research Institute for Pharmacy and Biochemistry in 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)

Quinta-Analytica s.r.o.

REaD VÚFB s.r.o.

VÚFB (Zentiva)

Certification

Good Laboratory Practice Certificate OECD GLP [C(97)186 Final]
Pharmaceuticals, medical devices and food additives

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.

Main Activities

Preclinical R&D

Cardiovascular disorders, diabetes, oncology, preclinical development of vaccines, neurodegenerative diseases

Comprehensive Toxicological Program

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

Laboratory Animals Breeding

Non-human primates, dogs, rodents

Summary Information

Structure of experimental work

R&D activities	27 %
Contract-based activities	73 %
GLP	61 %
Non-GLP	39 %

Staff structure

Total	50
University educated	18
High school educated	11

Structure of clients

Czech Republic	12 %
Europe	67 %
Asia	10 %
North America	9 %
Australia	2 %

Pharma/Biotech	74 %
Chem/Agrochem	8 %
Research org.	18 %



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R&D: Approved Projects - international

Framework Program 6 and 7:

SARS/FLU VACCINE: Development of a combined influenza/SARS vaccine
(Austria, Germany, Slovenia, Russia, Czech Republic)

FLUVAC: Live attenuated replication-defective influenza vaccine
(Austria, Germany, Russia, Slovenia, Czech Republic)

H5 VACCINE: Immunogenicity and protective efficacy of intranasal deINS1/H5N1 influenza vaccine
(Austria, Germany, Russia, UK, Czech Republic)

ANTIFLU: Innovative anti-influenza drugs excluding viral escape
(Denmark, France, Germany, Hungary, Israel, United Kingdom, Czech Republic)

OSTEOGROW: Novel bone morphogenetic protein-6 biocompatible carrier device for bone
(Austria, Bosnia and Herzegovina, Croatia, Czech Republic, Sweden)



R&D: Upcoming projects - international

Framework Program 7:

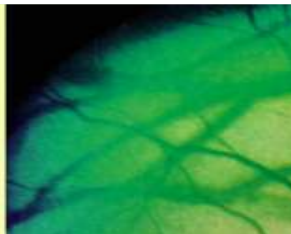
PedVacc HIV-TB: A phase I clinical trial in adults in Oxford of BCG.HIVconsv prime-MVA.HIVconsv.85A boost vaccine regimens against TB and breast-milk transmission of HIV-1

(United Kingdom – Oxford University, Czech Republic, Germany, USA)

SIMTB/SIMULT/SIMVAC: Development of Simultaneous Immunisation against Tuberculosis for Humans

(United Kingdom – Imperial College London, Australia, Czech Republic, Germany, The Netherlands)

MOTIF: Microbicide Optimization Through Innovative Formulation for Vaginal and Rectal Delivery (United Kingdom - King's College London, Czech Republic, France, Italy, USA)



National R&D Projects

Technology Agency of The Czech Republic:

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

Participants: Institut of Animal Physiology & Genetics CAS, BioTest s.r.o.)

Upcoming:

ODDC: Original Drug Development Center

Participants: Institut of Organic Chemistry and Biochemistry CAS, Institut of Chemical Technology, Institut of Experimental Medicine Cas, Institut of Physiology CAS, BioTest s.r.o., Quinta-Analytica s.r.o., Apigenex s.r.o.)

Collaboration within associations and clusters:

- **CzechBio** – Association of Czech biotechnology companies
- **MedChemBio Cluster** – Cluster of Medicinal Chemistry and Chemical Biology





R&D : Collaborative Advanced Projects

Projects conducted in collaboration with national and international partners

Experimental models of myocardial infarction - dogs

Liver ischemia/reperfusion injury – non-human primates

Hereditary melanoma model in miniature pigs - MeLiM strain

Transgenic chronic Huntingdon's diseases model – miniature pigs

Chronic traumatic spinal cord injury model – miniature pig



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Experimental models of myocardial infarction (beagle dog)

The occurrence of left ventricular dysfunction shortly following the onset of a myocardial infarction is mimicked by ligation of the left coronary artery which producing myocardial ischemia followed by heart reperfusion.

At the end of reperfusion, morphometric analysis of area at risk and area of infarction was performed using computerized program and the infarct size was determined by the weight of infarct over the weight of area at risk.

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

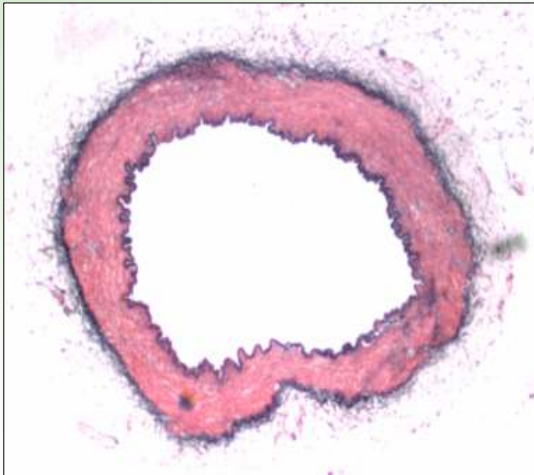


Myocardial section (Coomassie blue injected into *arteria coronaria*):
Dark blue – intact myocardium
Red – ischemia zone
White - infarctation zone



Vascular balloon injury model in rhesus monkeys

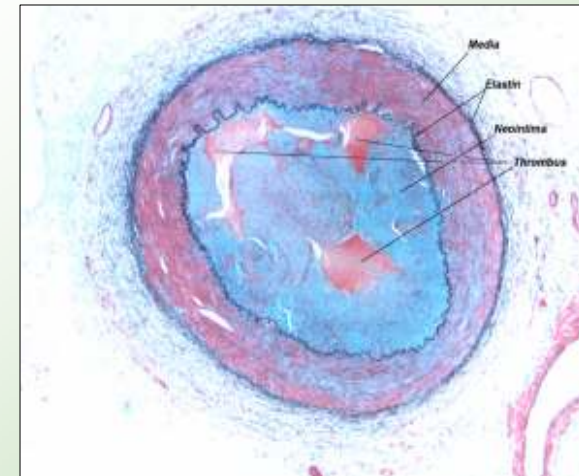
Balloon angioplasty is a common intervention for the treatment of blood vessel stenosis, particularly of the coronary vasculature. Similar procedure was used for repeated iliac artery occlusion. Inflated balloon causes significant trauma to the vascular endothelium, which is evidenced by an immediate loss of endothelial-dependent relaxation, and is itself associated with a concomitant induction of smooth muscle cell proliferation and neo-intima formation.



Non-injured iliac artery



The balloon catheter placement



Iliac artery after balloon injury



Experimental model of diabetes – macaque rhesus

Serum Glucose Concentration [mmol/l]							
	06/09	12/09	06/09	12/10	01/11	03/11	06/11
Females (pre-diabetic)	7.9 – 15,8	8,13 – 9,52	8,3 – 8,9	7,3 – 10,2	7,9 – 9,5	10,5 – 11,1	10,8 – 13,8
Males (pre-diabetic)	6,7 – 10,9	5,3 – 7,0	5,6 – 8,7	5,6 – 9,5	5,3– 8,1	5,9 – 11,3	6.8 – 11,5
BioTest Ref. Values (Males)*	3,9 – 5,5						
BioTest Ref. Values (Females)*	3,0- 4,7						
Clinical Laboratory Animal Medicine **	2,9 – 4,8						
The Laboratory Primate***	2,6 – 3,9						

* Reference Values, Clinical Chemistry Values, 2009: Unpublished data, BioTest s.r.o.

** K. Hrapkiewicz, L.Medina, Blackwell, 2007: Clinical Laboratory Animal Medicine, Iowa, USA

*** S. Wolfe-Coote, 2005: The Laboratory Primate, Elsevier Academic Press, USA



Chronic traumatic spinal cord injury model, pig

Computer-managed device has been developed providing **strictly repeatable spinal cord injury**, either in the **thoracal** or **lumbal region**, allowing the long lasting survival of paraplegic animals.

All essential reflexes (feeding, urination and defecation) are in function, so no infectious complications exist under laboratory conditions

The model is ready to use for:

- **stem cell therapy**
- **pharmacological approaches to a long-lasting treatment of paraplegia.**



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Contract-based Experimental Services

Genetic Toxicology

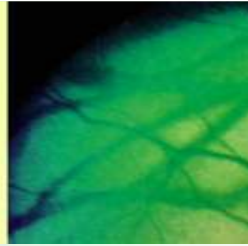
Gene mutation in bacteria (Ames test), *E.coli*, *S. Typhimurium*

Mammalian cells chromosome aberration, *in vitro*, human cells

Mammalian cell micronucleus test *in vitro*,

Mammalian micronucleus test *in vivo*, rodents

Cytotoxicity *in vitro*



Contract-based Experimental Services

Senzitization, Irritation, Local Tolerance

Skin/Eye irritation studies, in vivo, rabbit

Skin sensitization/Allergization studies, guinea pigs

Skin sensitization (Local Lymph Node Assay), mouse

**Local tolerance studies (topical application, post transplantation),
rodents, non-rodents**



Contract-based Experimental Services

General Toxicology, Pharmacology and Non-clinical Safety

Acute (Single dose) toxicity studies, rodents, non-rodents

MTD/DRF studies, rodents, non-rodents

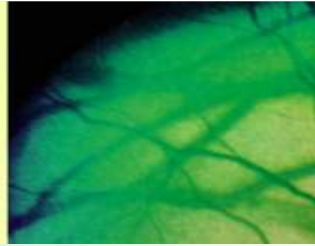
Sub-acute, sub-chronic, chronic toxicity studies, rodents, non-rodents

TK/PK/BA/BEQ/Biodistribution studies, rodents, non-rodents

Non-clinical safety studies, rodents, non-rodents

Safety pharmacology studies, non-rodents

Immunogenicity/Immunotoxicity studies, rodents, non-rodents



Contract-based Experimental Services

General Toxicology, Pharmacology and Non-clinical Safety

Non-clinical evaluation of anticancer pharmaceuticals, rodents, non-rodents

Pre-clinical safety evaluation of biotech-derived products, rodents, non-rodents

Preclinical evaluation of vaccines, rodents, non-rodents

Non-clinical implantation studies, rodents, non-rodents

Non-clinical local tolerance testing of medicinal products and medical devices, rodents, non-rodents



Contract-based Experimental Services

Toxicity to Reproduction

Prenatal developmental toxicity, rodents

Screening reproduction toxicity, rodents

One- and two-generation reproduction toxicity, rodents

DRF for embryo-fetal developmental study, rodents

Contract-based Experimental Services

Carcinogenicity

Dose selection for carcinogenicity studies, rodents

Carcinogenicity study, rodents

Combined chronic toxicity/carcinogenicity study, rodents

Biodistribution studies

Biodistribution studies after single/repeated dose, non-radiolabeled compounds, rodents, non-rodents

Biodistribution studies after single/repeated dose, radiolabeled compounds, rodents,



Contract-based Experimental Services

Experimental Animal models

Diabetes type II model, non-human primates

Diabetes type I model, rats

Chronic glaucoma model, beagle dogs

Osteoarthritis model, rabbits, dogs

Experimental infarction model, beagle dogs

Liver ischemia/reperfusion injury model, beagle dogs

Chronic traumatic spinal cord injury model, miniature pigs*

Acute Huntington disease, miniature pigs*



Laboratory Animal Breeding

Rodents

Rats (Wistar:Han), SPF quality

Mice (NMRI), SPF quality

Guinea Pigs (*Cavia aperea f. porcellus*)

Non-rodents

Rhesus macaques (*Macaca mulatta*), monitored quality

Beagle dogs, monitored quality

References

Affiris, Austria

Aginko AG, Switzerland

Avir Green Hills Biotechnology,
Austria

Baxter Biosciences, Austria

Bio-Assistance, Canada

CINIC Chemicals, China

Gelesis Inc., USA

Ikaria Inc., USA

ICRC/NUSA, CZ-USA

Immune System Key, Israel

King's College London, UK

Lesaffre, France

Mabion, Poland

Medicine Development, Australia

Max-Planck Inst. of Inf. Biol. Germany

Midatech, Switzerland

Novo Nordisk, Denmark

Oncos Therapeutics, Finland

Panacea Biotech, India

Pharmasafe, Switzerland

Pre-clinical Consultancy, Israel

Rottapharm, Italy

Sun Pharmaceuticals, India

Vetcare Oy, Finland



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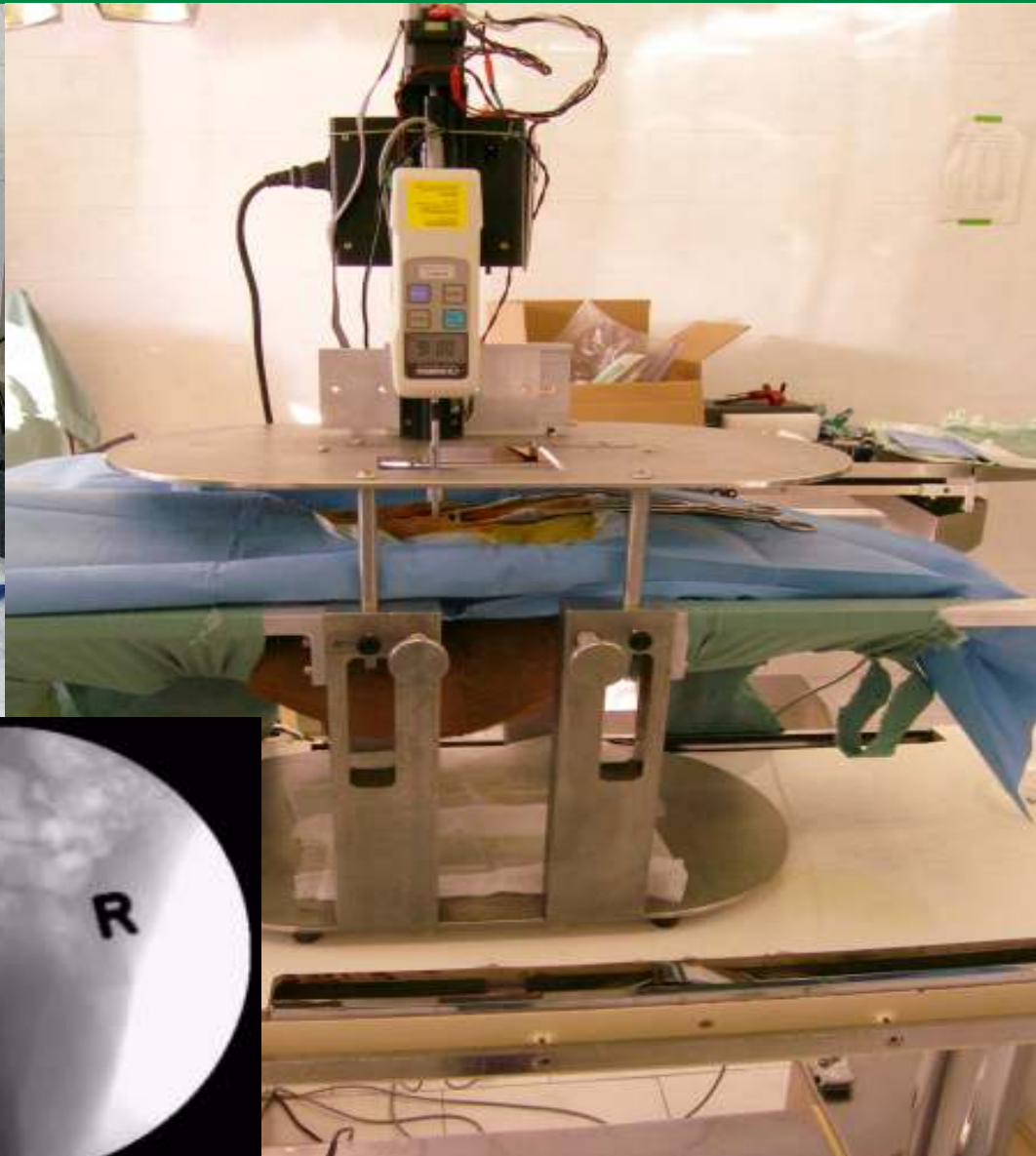
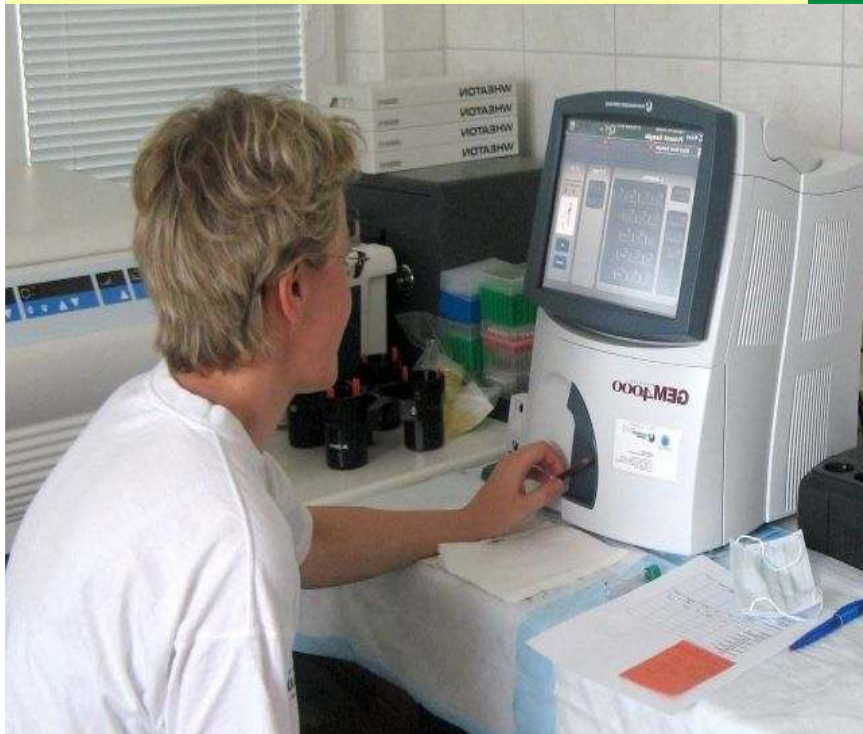
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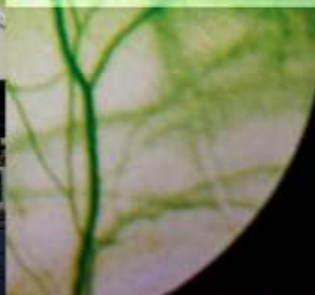
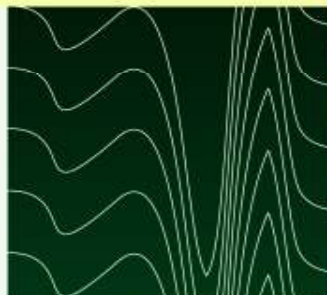
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