

# MEDITOX

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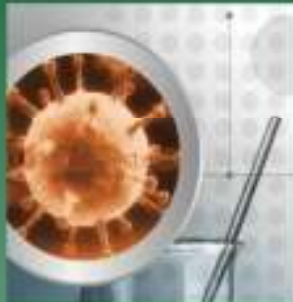
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GLP certificate holder

Hemodynamic  
laboratory

Huntington's disease  
model

Diabetes/Obesity  
model

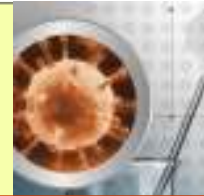


[www.meditox.eu](http://www.meditox.eu)

- Preclinical research and development
- Comprehensive preclinical and toxicological program
- Animal models for selected human diseases
- Accredited breeding facility for laboratory animals

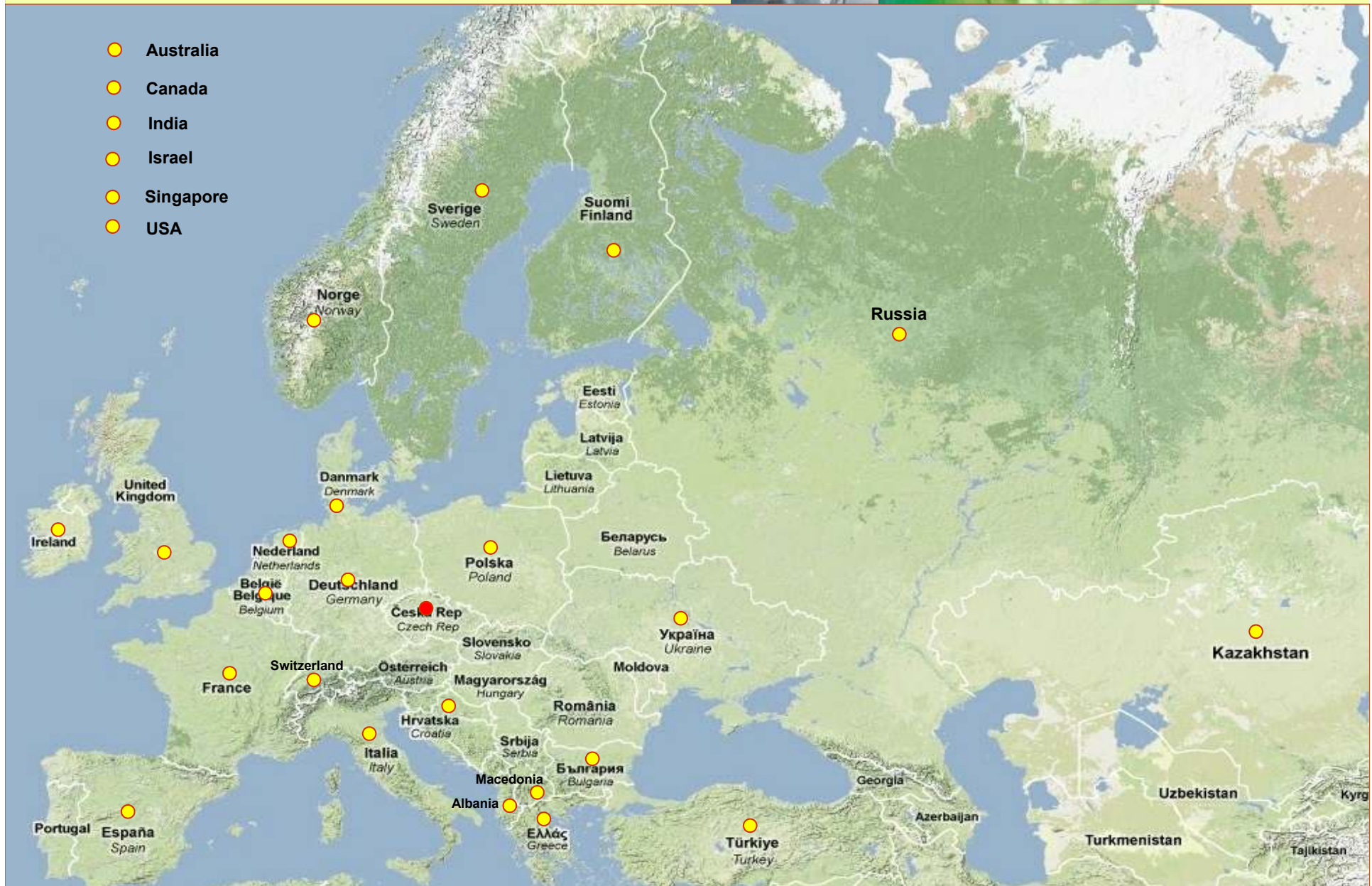
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- Australia
- Canada
- India
- Israel
- Singapore
- USA







## 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)

**April 1, 2013: Change the company name 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

### Laboratory Animals 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**

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

<b>R&amp;D activities</b>	<b>31 %</b>
<b>Contract-based activities</b>	<b>69 %</b>
<b>GLP</b>	<b>58 %</b>
<b>Non-GLP</b>	<b>42 %</b>

### Staff structure

<b>Total number</b>	<b>50</b>
<b>University educated</b>	<b>30 %</b>
<b>High school educated</b>	<b>63 %</b>

### Structure of clients

<b>Czech Republic</b>	<b>15 %</b>
<b>Europe</b>	<b>65 %</b>
<b>Asia</b>	<b>9 %</b>
<b>North America</b>	<b>9 %</b>
<b>Australia</b>	<b>2 %</b>
<b>Pharma/Biotech</b>	<b>68 %</b>
<b>Chem/Agrochem</b>	<b>11 %</b>
<b>Research org.</b>	<b>21 %</b>



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## Selected R&D Projects - international

### Framework Program 7:

**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)

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

(Czech Republic, France, Italy, United Kingdom)

**HELICOVAXOR: Development of an oral Helicobacter Pylori vaccine**

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

**UNIVERSAL VACCINE: Synthetic self-replicating RNA vaccines targeted to dendritic cells as „universal“ influenza and future generic vaccines**

(Czech Republic, France, Germany, Norway, Russia, Switzerland)





## 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.)**

### **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**





## 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





## Experimental model of diabetes – macaque rhesus

Serum Glucose Concentration [mmol/l]							
	09/10	01/11	06/11	12/11	01/12	06/12	12/12
Females (pre-diabetic)	8.9 – 15,8	8,13 – 9,52	8,3 – 8,9	8,3 – 10,2	8,9 – 9,5	9,5 – 11,1	10,8 – 13,8
Males (pre-diabetic)	6,7 – 10,9	5,3 – 7,0	5,6 – 8,7	7,6 – 9,5	6,3– 8,1	6,9 – 11,3	6.8 – 11,5
<b>BioTest Ref. Values (Males)*</b>	<b>3,9 – 5,5</b>						
<b>BioTest Ref. Values (Females)*</b>	<b>3,0- 4,7</b>						
<b>Clinical Laboratory Animal Medicine **</b>	<b>2,9 – 4,8</b>						
<b>The Laboratory Primate***</b>	<b>2,6 – 3,9</b>						

\* 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.**





## Contract-Based Experimental Services

### General Toxicology, Pharmacology and Non-Clinical Safety

**Acute (Single dose) toxicity, MTD/DRF, sub-acute, sub-chronic, chronic toxicity (rodents and non-rodents)**

**PK/BA/BEQ/Biodistribution studies (rodents & non-rodents)**

**Immunogenicity/Immunotoxicity studies (rodents & non-rodents)**

**Safety pharmacology studies (non-rodents)**

**Non-clinical evaluation of anti-cancer pharmaceuticals (rodents & non-rodents)**

**Pre-clinical safety evaluation of biotech-derived products (rodents & non-rodents)**

**Non-clinical implantation studies (rodents & non-rodents)**

**Biocompatibility and non-clinical local tolerance of medicinal products**



## Contract-Based Experimental Services

### Genetic Toxicology, Cytotoxicity

**Gene mutation in bacteria (*in vitro*)**

**Mammalian cell chromosome aberration (*in vitro*)**

**Mammalian cell micronucleus test (*in vitro* & *in vivo*)**

### Local Effects

**Skin/Eye irritation (*in vivo*)**

**Skin sensitization/Allergization (GMPT, Buehler test, LLNA)**

**Local tolerance studies (rodents & non-rodents)**

**Implantation studies (rodents & non-rodents)**



## Contract-Based Experimental Services

### Toxicity to Reproduction

**Screening reproduction toxicity (rodents)**

**Prenatal developmental toxicity (rodents)**

**DRF for embryo-fetal developmental study (rodents)**

**One- and Two-generation reproduction toxicity (rodents)**

**Combined toxicity/reproduction studies (rodents)**

### Carcinogenicity

**Dose selection for carcinogenicity (rodents)**

**Carcinogenicity studies (rodents)**

**Combined toxicity and carcinogenicity studies (rodents)**

### Biodistribution studies

**Single, repeated dose, non-labeled compounds (rodents & non-rodents)**





## Experimental Services

### Animal models of selected human diseases

**Diabetes type II model**, non-human primates

**Diabetes type I model**, rats

**Chronic glaucoma model**, dogs

**Experimental infarction model**, beagle dogs

**Liver ischemia/reperfusion injury model**, beagle dogs

**Chronic traumatic spinal cord injury model**, miniature pigs

**Acute contact dermatitis**, pigs

**Models under preparation: Diabetes in dogs**

**Obesity model, mice**

**Alzheimer disease, mice**

**Arthritis model, rats**



## 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

**Baxter Biosciences**, Austria

**Bio-Assistance**, Canada

**CINIC Chemicals Europe**, France

**Chanelle Group** (Ireland)

**Dechra Veterinary Products**, UK

**Gelesis Inc.**, USA

**Ikaria Inc.**, USA

**Immune System Key**, Israel

**Imperial College London**, UK

**JSC Pharmstandard**, Russia

**King's College London**, UK

**KRKA**, Croatia

**Lesaffre**, France

**Lupin Pharma**, India

**Mabion**, Poland

**Max-Planck Inst. of Inf. Biol.** Germany

**Midatech**, Switzerland

**NanoBioMatters Industries**,  
Spain/Japan

**NovoNordisk**, Denmark

**OCT Clinical Trials**, USA

**Oncos Therapeutics**, Finland

**Panacea Biotech**, India

**Pharmathen**, Greece

**Sanofi Group** (Zentiva)

**Sun Pharmaceuticals**, India

**Vetcare Oy**, Finland and more...



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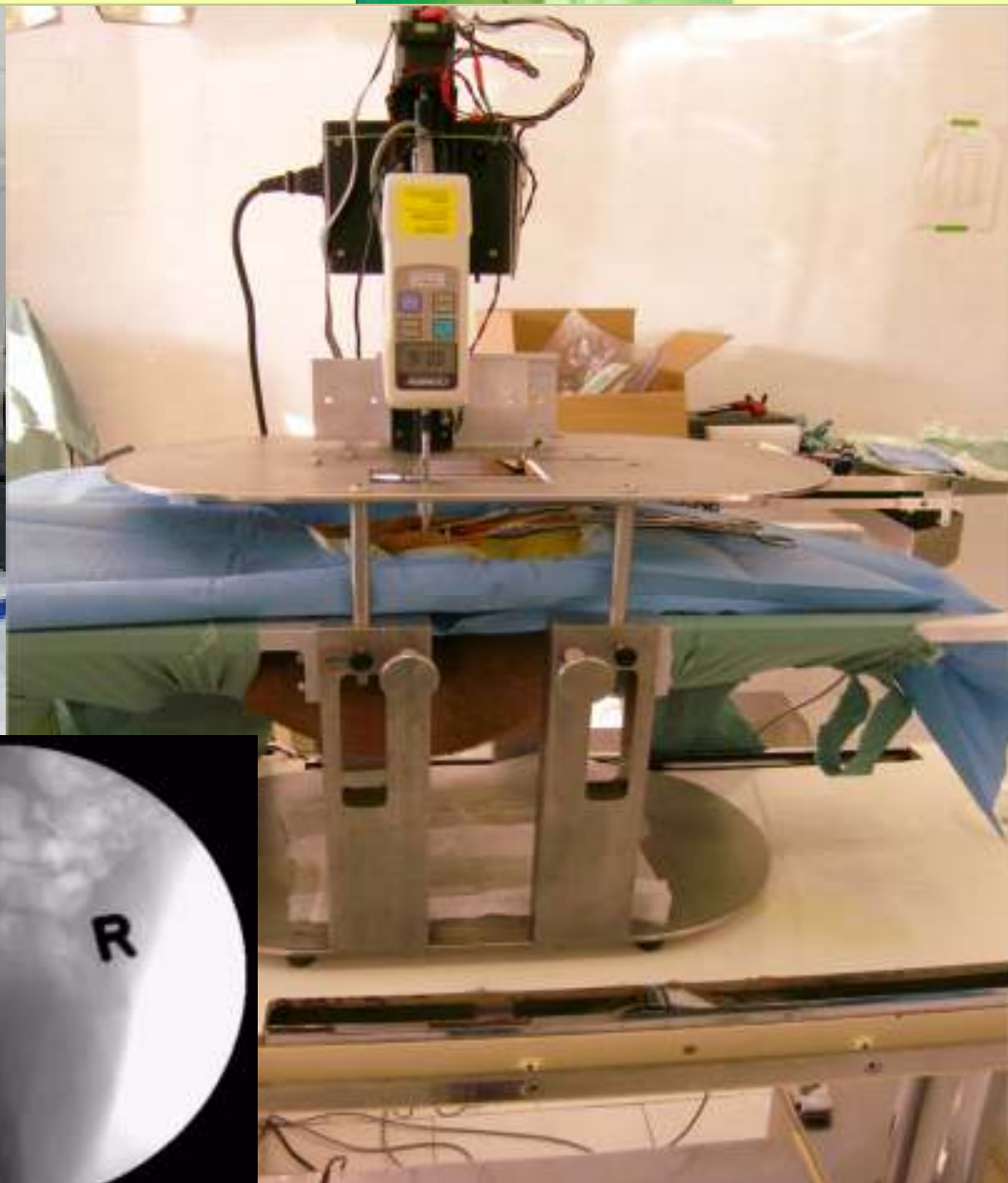


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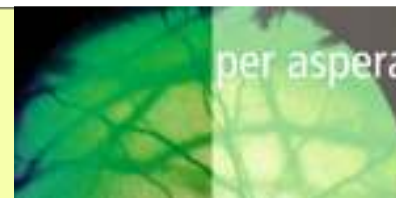
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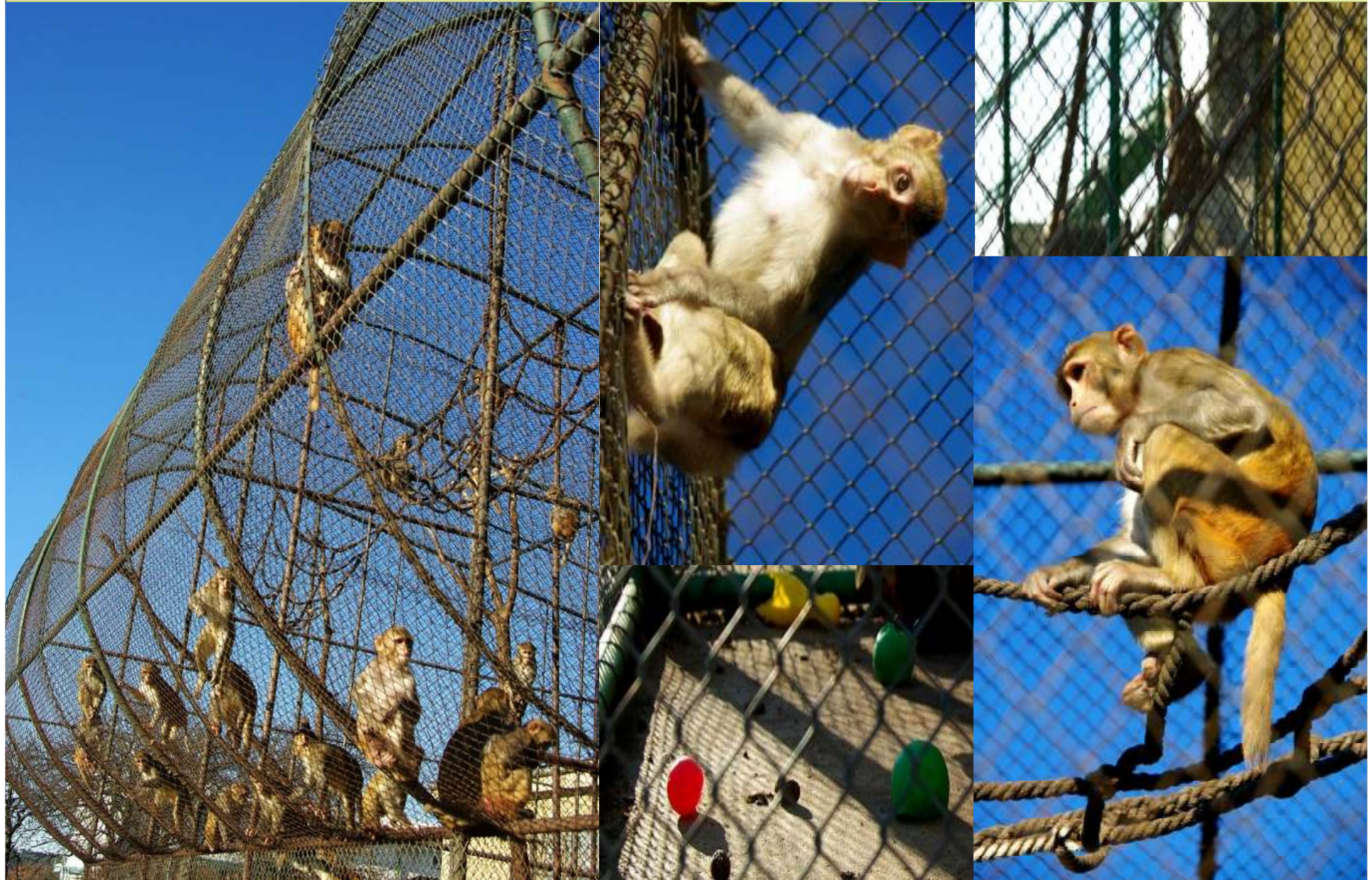


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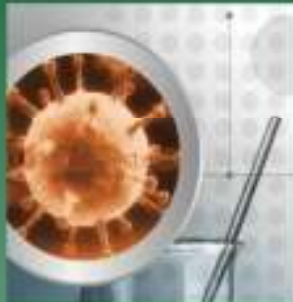
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Huntington's disease  
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Diabetes/Obesity  
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## Thank you for attention

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- Preclinical research and development
- Comprehensive preclinical and toxicological program
- Animal models for selected human diseases
- Accredited breeding facility for laboratory animals