

MEDITOX	MEDITOX CAPABILITIES
MediTox s.r.o. Pod Zámkem 279 CZ-281 25 Konárovice	

Species:	Non-rodent: Dogs, cats, rabbits, ferrets, pigs/mini pigs, NHP Rodent: Mice, rats, hamsters, guinea pigs
Way of administration:	Oral, buccal, sub-lingual, intra-venous, intra-muscular, intra-peritoneal, intra-cardial, intra-dermal, intra-nasal, intra-tracheal, intra-articular, intra-vitreous, rectal, vaginal, dermal, sub-cutaneous, ocular, implantation (into the muscle, sub-cutis, bone)

I. HUMAN MEDICINE AREA

General toxicology

Exploratory		
Test/Study	Specification	Method
Maximum tolerated dose (MTD)	Rodents, non-rodents Clinical and clinical-laboratory observation, gross pathology	EMA/CHMP/SWP/81714/2010, CHMP/SWP/302413/08
Dose range finding study (DRF, 7 – 90 days)	Rodents, non-rodents Repeated administration, 7d/wk exposure, clinical and clinical-laboratory examination, gross pathology, optional histopathology	CPMP/SWP/1042/99 Rev. 1 Corr.
Pilot, proof-of concept studies	Rodents, non-rodents Depends on the study range	-
Regulatory		
Test/Study	Specification	Method
Acute (Single dose) toxicity	Rodents Limit test/Full study	OECD 420, 423, 425, 402, EMA/CHMP/SWP/81714/2010
Acute (single dose) inhalation toxicity <i>Note: subcontracted</i>	Rodents	OECD 403, 436
Extended single dose toxicity study	Rodents Clinical and clinical-laboratory observation, gross and histopathology	CPMP/ICH/286/95, ICH M3(R2)
Sub-acute toxicity studies (7 – 28 days)	Rodents, non-rodents Repeated administration, 7d/wk exposure, clinical and clinical-laboratory examination, gross pathology, full set of histopathology Optionally: TK sampling, recovery	CPMP/SWP/1042/99 Rev. 1 Corr, OECD 407, 410
Sub-chronic toxicity studies (90 days) rodents, non-rodents	Rodents, non-rodents Repeated administration, 7d/wk exposure, clinical and clinical-laboratory examination, gross pathology, full set of histopathology Optionally: TK sampling, recovery	CPMP/SWP/1042/99 Rev. 1 Corr, OECD 408, 409, 411
Chronic toxicity study (6 months)	Rodents, non-rodents Repeated administration, 7d/wk exposure, clinical and clinical-laboratory examination, gross pathology, full set of histopathology Optionally: TK sampling, recovery	CPMP/SWP/1042/99 Rev. 1 Corr, CPMP/ICH/300/95 OECD 452
Chronic toxicity study (9 – 12 months),	Non-rodents Repeated administration, 7d/wk exposure,	CPMP/SWP/1042/99 Rev. 1 Corr, CPMP/ICH/300/95

MEDITOX	MEDITOX CAPABILITIES
MediTox s.r.o. Pod Zámkem 279 CZ-281 25 Konárovice	

	clinical and clinical-laboratory examination, gross pathology, full set of histopathology Optionally: TK sampling, recovery	OECD 452
--	--	----------

Genetic Toxicology

Test/Study	Specification	Method
Gene mutation in bacteria <i>Note: subcontracted</i>	Ames test (plate incorporation method)	OECD 471, ICH S2(R1)
Mammalian chromosome aberration <i>in vitro</i> <i>Note: subcontracted</i>	300 metaphase chromosomes	OECD 473, ICH S2(R1)
Erythrocyte micronucleus <i>in vivo</i> , rodents <i>Note: males only, subcontracted</i>	mouse, males, 4000 cels/animal	OECD 474, ICH S2(R1)
Micronucleus test <i>in vitro</i> <i>Note: subcontracted</i>	Three dose levels	OECD 487, ICH S2(R1)
Comet assay <i>in vivo</i> (rodents) <i>Note: subcontracted</i>	3 organs	OECD 489
Mouse lymphoma assay <i>Note: subcontracted</i>	L5178Y (mutation TK)	OECD 490
Cytotoxicity <i>in vitro</i> <i>Note: subcontracted</i>	Murine fibroblasts	ISO 10993-5

Local Effects (Irritation, Sensitization, Local Tolerance)

Test/Study	Specification	Method
Skin irritation <i>in vivo</i>	Rabbit Observations at 24h, 48h, 72h, (-7d & 14d)	OECD 404
Skin irritation <i>in vitro</i> <i>Note: subcontracted</i>	RHE	OECD 431, 439
Eye irritation <i>in vivo</i>	Rabbit Observations at 24h, 48h, 72h, (7d, 14d & 21d)	OECD 405
Eye irritation <i>in vitro</i> <i>Note: subcontracted</i>	BOCP	OECD 437
Skin sensitization: LLNA <i>Note: subcontracted</i>	Mouse Reduced LLNA/Individual nodes	OECD 429
Skin sensitization <i>in vivo</i>	Magnusson, Buehler method	OECD 406
<i>In vitro</i> skin sensitization <i>Note: subcontracted</i>	Direct Peptide Reactivity Assay	OECD 442C
	Keratinosens	OECD 442D
	h-CLAT	OECD 442E
Non-clinical local tolerance testing of medicinal products, rodents, non-rodents	Guinea pig Dermal, ophthalmic, vaginal, rectal, etc.	CPMP/SWP/2145/00, ISO 10993
Local tolerance after implantation	Rodents, non-rodents Implantation into sub-cutis, muscle, bone, intra-cardial, etc. including histomorphometry	ISO 10993-6

MEDITOX	MEDITOX CAPABILITIES
MediTox s.r.o. Pod Zámkem 279 CZ-281 25 Konárove	

Safety Pharmacology

Test/Study	Specification	Method
Safety Pharmacology: CNS <i>Note: Safety pharmacology end-points can be included into repeated dose toxicity study</i>	Rodents Modified Irwin test, rodents Single or repeated dose	ICH S7
Safety Pharmacology: CVS <i>Note: Safety pharmacology end-points can be included into repeated dose toxicity study</i>	Rat, Dog Single or repeated dose	ICH S7
Safety Pharmacology: respiratory <i>Note: subcontracted</i>	Rat, Head-out plethysmography	ICH S7

Pharmacokinetics/Toxicokinetics/Bioavailability

Test/Study	Specification	Method
TK/PK/BA/studies	Rodents, non-rodents Administration, blood sampling, samples preparation	CPMP/ICH/384/95, 3BS11A, OECD 417,
	Implementation and validation of analytical method (subcontracted)	
	Development, implementation and validation of analytical method (subcontracted)	
	Sample analysis and results evaluation and statistics (subcontracted)	

Non-Clinical Safety

Test/Study	Specification	Method
Nonclinical evaluation of the potential for delayed ventricular repolarization	Rat, rabbit, dog SD/RD administration, ECG, body temperature, blood pressure recording	CPMP/ICH/423/02, CPMP/ICH/539/00, ICH S7A, ICH S7B
Non-clinical safety studies for the conduct of human clinical trials for pharmaceuticals	Rodent, non-rodents SD/RD administration, clinical, clinical-laboratory examination, gross pathology, histopathology	CPMP/ICH/286/95, ICH M3(R2)
Immunotoxicity/Immunogenicity studies	Rodents, non-rodents SD/RD administration, complex evaluation of clinical, clinical-laboratory, gross pathology, histopathology data in terms of immunostimulation, immunosuppression or immunomodulation	CHMP/ICH/167235/04
Preclinical safety evaluation of biotechnology-derived products	Rodents, non-rodents SD/RD administration, clinical, clinical-laboratory examination, gross pathology, histopathology	CPMP/ICH/302/95, EMA/CHMP/ICH/731268/1998, ICH S6(R1)
Preclinical pharmacological and toxicological testing of vaccines	Rodents, non-rodents SD/RD administration, clinical, clinical-laboratory examination, gross pathology, histopathology	CPMP/SWP/465/95, CVMP/IWP/52/97
Nonclinical evaluation for anticancer pharmaceuticals	Rodents, non-rodents Repeated dose administration, clinical, clinical-laboratory examination, gross pathology, histopathology	CHMP/ICH/646107/2008, ICH S9

MEDITOX	MEDITOX CAPABILITIES
MediTox s.r.o. Pod Zámkem 279 CZ-281 25 Konárovice	

Efficacy

Test/Study	Specification	Method
Antiviral efficacy/Immunogenicity studies	Mouse, rabbit, ferret Efficacy of anti-influenza therapy (vaccines, small molecules)	EMA/CHMP/VWP/457259/2014, EMA/CHMP/VWP/141697/2009
Antiglaucoma efficacy	Dog Efficacy of antiglaucoma therapy	Model of chronic glaucoma
Efficacy of osteoarthritis treatment	Dog Efficacy of antiglaucoma therapy	Osteoarthritis model

Biodistribution

Test/Study	Specification	Method
Biodistribution studies after single/repeated administration, non-labeled compounds, biological part (<i>analytical part is subcontracted</i>)	Rodents, non-rodents Biodistribution in blood, urine, feces and tissues, LCMS, HPLC, qPCR	OECD 417, CPMP/ICH/385/95, 3BS11A

Models Available

Chronic glaucoma model in dogs
Influenza model in ferrets
Osteoarthritis model in rabbits, dogs
Acute contact dermatitis model in pigs

II. VETERINARY MEDICINE and ANIMAL FEED AREA

Test/Study	Specification	Method
Target animal safety studies	Dog, cat, rabbit D administration, 7d/wk exposure, clinical and clinical-laboratory examination, gross pathology, full set of histopathology, if requested	VICH GL43
Bioequivalence studies	Dog, cat rabbit Administration, blood sampling, samples preparation	VICH GL 52
	Implementation and validation of analytical method (<i>subcontracted</i>)	
	Development, implementation and validation of analytical method (<i>subcontracted</i>)	
	Sample analysis and results evaluation and statistics (<i>subcontracted</i>)	
Immersion/Washout study	Dogs Immersion, water & blood sampling, samples preparation	EMA guidelines VICH (1998A), VICH (1998B) and EMA guideline (2012).
	Implementation and validation of analytical method (<i>subcontracted</i>)	
	Development, implementation and validation of analytical method	

MEDITOX	MEDITOX CAPABILITIES
MediTox s.r.o. Pod Zámkem 279 CZ-281 25 Konárovice	

Wipe test	(subcontracted)	EMA/CVMP/SWP/ 721059/2014
	Sample analysis and results evaluation and statistics (subcontracted)	
	Dogs, cats Wiping, samples collection	
	Implementation and validation of analytical method (subcontracted)	
	Development, implementation and validation of analytical method (subcontracted)	
	Sample analysis and results evaluation and statistics (subcontracted)	

Feed Testing

Test/Study	Specification	Method
Palatability study	Rodents, non-rodents Palatability testing in laboratory animals	EFSA
Feed safety studies	RD administration, 7d/wk exposure, clinical and clinical-laboratory examination, gross pathology, full set of histopathology, if requested	VICH/ EFSA

III. MEDICAL DEVICE AREA

Test/Study	Specification	Method
Tests for genotoxicity, carcinogenicity and reproductive toxicity	Mutagenicity in bacteria, chromosomal aberration test, micronucleus test, etc.	ISO 10993-3, OECD 471, 473, 475, 474, 476, 487, 489
Tests for <i>in vitro</i> cytotoxicity	MTT	ISO 10993-5
Tests for local effects after implantation	Rodents, non-rodents Implantation to sub-cutis, muscle and bone	ISO 10993-6
Tests for irritation and skin sensitization	Eye, skin, mucosa	ISO10993-23, OECD 404, 405, 406, 429, 431, 438
Tests for systemic toxicity	Rodents, non-rodents Acute, sub-acute, sub-chronic, chronic	ISO 0993-11

III. FACILITIES AVAILABLE

Biosafety level II for small animals (up to the size of rabbit), GMO handling
In house clinical pathology (hematology, serum chemistry, urinalysis)
In house gross pathology and histopathology
Veterinary surgery operation