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LPS- Pulmonary Inflammation
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Stress-Induced Hyperthermia
Stress-Induced Corticosterone
Tail Suspension
Tail-Flick
von Frey/Carrageenan Sensitivity
Weight Gain

Cardiovascular:

Assay	Validating Compound	Parameters	Species	Comments
Bleeding Time *	Heparin	Time to bleeding cessation	Mouse, Rat	Short lead time required, Good reproducibility
Blood Pressure Tail Cuff	Nifedipine	Blood pressure and heart rate	Rat	Short lead time required, Group size n>12
Hypertension/Telemetry	Candesartan	SHR Rats Blood Pressure/MAP Heart Rate	Mouse, Rat	Surgically complex

Gastrointestinal:

Assay	Validating Compound	Parameters	Species	Comments
Colonic Propulsion *	Morphine	Latency to colonic expulsion of glass bead	Mouse, Rat	Short lead time required, Good reproducibility
DSS – Model of Colitis *	Cyclosporin A	Body Weight Gastrointestinal distress	Mouse	Short lead time required, Good reproducibility
Fecal Output *	Morphine	Fecal pellet count	Mouse, Rat	Short lead time required, Good reproducibility
Gastrointestinal Transit *	Morphine	Intestinal distance traveled of gavage – administered charcoal bolus	Mouse, Rat	Short lead time required, Good reproducibility
IBS and Acetylcholine Writhing *	Morphine	Time to writhing onset Number of writhes	Mouse, Rat	Short lead time required, Good reproducibility
Morphine-Induced Constipation *	Naloxone	Latency of colonic expulsion of glass bead	Mouse, Rat	Short lead time required, Good reproducibility

Hair Growth and Dermatitis:

Assay	Validating Compound	Parameters	Species	Comments
Allergic Contact Hypersensitivity *	Dexamethasone	Swelling of ears sensitized to oxazolone, PPD, or DNFB Clinical evaluation of ear redness, Cytokine/IL levels in ear biopsies, INF - γ	Mouse, Rat	Short lead time required, Good reproducibility
Delayed – Type Hypersensitivity	Dexamethasone	Footpad thickness after immunogenic challenge	Mouse, Rat	Short lead time required, Good reproducibility
Hair Growth Assay	Minoxidil	Hair growth score, Time and magnitude	Mouse	Chronic Model
Sebum Production *	N/A	Sebum production, Fur water retention	Mouse	No positive control available
Pruritis Scratching	U-50,488	Total scratching events over 30-minute period	Mouse	Variable duration depending on pruritis-inducing agent

Inflammation and Arthritis:

Assay	Validating Compound	Parameters	Species	Comments
Acute Nephritis	DL-propargylglycine (PAG)	Blood (BUN, CRE, Sodium) and urine (CRE, Protein) chemistries	Rat	Short lead time required
Acute Pancreatitis	DL-propargylglycine (PAG)	Markers of pancreatic injury (Serum Amylase, Pancreatic Myeloperoxidase)	Mouse	Short lead time required
Allergic Contact Hypersensitivity *	Dexamethasone	Swelling of ears sensitized to oxazolone, PPD, or DNFB Clinical evaluation of ear redness, Cytokine/IL levels in ear biopsies, INF- γ	Mouse, Rat	Short lead time required, Good reproducibility
Capsaicin Hyperalgesia Assay	Morphine	Pain responsiveness after Capsaicin inflammation	Rat	Short lead time required, Good reproducibility
Collagen Induced Arthritis	Dexamethasone	Clinical evaluation of paw and joint inflammation	Mouse, Rat	Strain sensitive, Short lead time required, Good reproducibility
Delayed Type Hypersensitivity*	Dexamethasone	Footpad thickness after immunogenic challenge	Mouse, Rat	Short lead time required, Good reproducibility
EAE Model of Multiple Sclerosis *	FTY 720	Clinical Scores Body weight	Mouse, Rat	Strain and supplier sensitive Good reproducibility
Formalin Analgesia Assay*	Oxycodone	Duration of Phase I (acute) pain, Duration of Phase II (delayed) pain	Mouse, Rat	Short lead time required, Good reproducibility
LPS – Pulmonary Inflammation *	Dexamethasone	Cytokine and MCP-1 levels in dissected lung tissue, Cellular infiltrate analysis	Mouse, Rat	Acute model, Short lead time required, Good reproducibility
LPS – Systemic Inflammation*	Dexamethasone	TNF- α and IL-6 blood levels after lipopolysaccharide challenge	Mouse, Rat	Acute model, Short lead time required, Good reproducibility
Monocyte Infiltration *	Dexamethasone	MCP-1 levels from peritoneal lavage, Differentials	Mouse, Rat	Short lead time required, Good reproducibility
Pulmonary Allergic Asthma*	Dexamethasone	Cytokine and MCP-1 levels in dissected lung tissue, Cellular infiltrate analysis	Mouse, Rat	<i>Ovalbumin</i> Chronic Model, Short lead time required, Good reproducibility
Zymosan-A Induced Peritonitis	Dexamethasone	Zymosan-A induces leukocyte accumulation in the peritoneum	Mouse	Short lead time required, Good reproducibility

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Metabolic:

Assay	Validating Compound	Parameters	Species	Comments
db/db Mouse Model	Rosiglitazone	Multiple parameters: Chronic glucose, Hormones, HbA1c, pancreatic insulin, IHC	Mouse	Chronic, Good reproducibility
DEXA *	N/A	Bone parameters and body composition (fat and lean) parameters	Mouse	Coupled with high fat diet, Good reproducibility
Diet Induced Obesity	Rimonabant	Body composition (fat and lean), Weight change over time, Glycemic control parameters (FPG, OGTT, ITT)	Mouse, Rat	Good reproducibility
Diet Induced Obesity/High-Fat Diet *	Rimonabant	Quantity of food ingested per day and per gram of body weight, Weight change over time, Weight change from initial measurement, DEXA analysis, Serum markers for Leptin, Insulin, and Adiponectin	Mouse, Rat	Can be coupled with multiple assays, Short lead time required, Good reproducibility
Euglycemic/Hyperglycemic Clamp Study	N/A	Hyperinsulinemic euglycemic clamp, Glucose infusion rate to maintain euglycemia with constant insulin infusion rate	Mouse, Rat	Gold standard measure of insulin sensitivity
Food Intake *	Imipramine	Quantity of food ingested per day and per gram of body weight, Food ingested after fasting	Mouse, Rat	Short lead time required, Good reproducibility
Insulin Tolerance Test (ITT)*	Insulin	Glucose response to insulin	Mouse, Rat	Can be coupled with multiple assays Short lead time required, Good reproducibility
mHFD-Induced NASH Model	Obeticholic Acid	Multiple parameters: Weight change from initial measurement, Glycemic control parameters (OGTT, ITT), Fasting ALT and Serum Triglycerides	Mouse	Good reproducibility
mHFD-Induced NASH Model/Enhanced Fibrosis	Obeticholic Acid	Multiple parameters: Weight change from initial measurement, Glycemic control parameters (OGTT, ITT), Serum Triglycerides/Cholesterol, ALT/AST levels, Hydroxyproline levels	Mouse	Variation of mHFD-Induced NASH model utilizing CCL4 Good reproducibility

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Assay	Validating Compound	Parameters	Species	Comments
Metabolic Hormone Levels *	Rimonabant	Leptin, insulin, adiponectin, c-peptide, etc. in response to multiple challenges (high fat diet, drug treatment, acute/chronic)	Mouse, Rat	Coupled with multiple metabolic assays, Short lead time required, Good reproducibility
ob/ob Mouse Model	Rosiglitazone	Multiple parameters: chronic glucose, hormones, HbA1c, pancreatic insulin, IHC	Mouse	Chronic, Good reproducibility
Oral Glucose Tolerance Test (OGTT) *	Metformin	Glucose levels over a trial period after glucose challenge, Pre/Post- High fat diet regimen	Mouse, Rat	Can be coupled with high fat diet model, Short lead time required, Good reproducibility
Streptozotocin-Induced Diabetes	Insulin	Multiple parameters, Chronic glucose, hormones, HbA1c, Diuresis and Nephropathy	Mouse, Rat	Metabolic Type I Diabetes, Highly specialized, Well - characterized
Weight Gain *	Imipramine	Weight change from initial measurement, Weight change per day	Mouse, Rat	Short lead time required, Good reproducibility
ZDF Rats	Insulin	Multiple parameters, Chronic glucose, hormones, HbA1c, pancreatic insulin, IHC	Rat	Short lead time required, Good reproducibility

Motor Function:

Assay	Validating Compound	Parameters	Species	Comments
Electromyography (EMG)	N/A	Flexor (C-fiber), Ia, H reflex aptitudes	Rat	Highly specialized capability
Grip Strength *	N/A	Force exerted to hold onto a wire screen	Mouse, Rat	ALS model Fast turn-around time, Can be coupled with other assays
Harmaline-Induced Tremor	Propranolol	Body tremor (tremor ratio)	Mouse, Rat	Fast turn-around time, Good reproducibility
Locomotor and Open Field Activity *	Risperidone	Locomotor parameters in an automated open-field	Mouse, Rat	Typically coupled with other assays, Short lead time required, Good reproducibility
Motor Evoked Potentials (CMAP)	N/A	Tibialis anterior and plantaris response latencies, Behavioral evaluation (limp splay, toe spread)	Mouse	ALS model Strain and supplier sensitive, Good reproducibility
Pole Test *	N/A	Time to T-turn	Mouse	Fast turn-around time, Can be repeated over time, Good reproducibility
Rotarod *	Haloperidol	Coordination, Acceleration	Mouse, Rat	Primarily utilized as pharmacology safety assay

Neurology:

Assay	Validating Compound	Parameters	Species	Comments
6-Hz Psychomotor Seizure	Valproate	Seizure exhibition	Mouse	Epilepsy Fast turn-around time, Good reproducibility
6-OHDA Lesion	Amantadine	Rotational behavior, Dopaminergic markers, Dyskinesias	Rat	Newly developed, Neurodegenerative symptomatic Parkinson's disease model
Audiogenic Seizure/FMR1 Knockout	R-baclofen	Locomotor activity, Seizure (score 0-4)	Mouse	Fragile X Model Short lead time required, Good reproducibility
Catalepsy *	Haloperidol	Reversal of haloperidol-induced cataleptic response	Mouse	Newly developed
Experimental Autoimmune Encephalomyelitis (EAE)	FTY 720	Clinical scores, Body weight	Mouse, Rat	Strain and supplier sensitive, Good reproducibility
EEG Pro- and Anti-Convulsant Evaluation	Diazepam, Pentylenetetrazol	Sub-clinical seizure threshold in response to seizure-inducing agents	Mouse, Rat	Highly specialized capability
L-DOPA Induced Dyskinesia	Amantadine	Axial, limb and orolingual AIMS	Rat	Neurodegenerative model of Parkinson's Disease, Short lead time required, Good reproducibility

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Lithium Pilocarpine Status Epilepticus	Diazepam, Pilocarpine	Cortical EEG activity in response to pilocarpine-induced SE	Rat	CNS/Epilepsy, Short lead time required, Good reproducibility
Maximal Electroshock *	Phenytoin	Seizure (presence/absence)	Mouse	6 Hz seizure, Short lead time required, Good reproducibility
MPTP-induced Parkinson's Disease *	L-deprenyl	Locomotor parameters in an automated open-field apparatus, Striatal dopamine levels, Dopamine cell number (TH staining; substantia nigra)	Mouse	Neurodegenerative model of Parkinson's Disease, Strain and supplier sensitive, Short lead time required, Good reproducibility
Pentylentetrazol-Induced Seizures *	Diazepam	Time to initial colonic seizure, Time to initial tonic seizure, EEG measurements	Mouse, Rat	CNS/Epilepsy, Short lead time required, Good reproducibility
Rett Syndrome Neurodevelopment Model	N/A	Locomotor, Respiration, Seizure, Mortality	Mouse	Neurodegeneration/Rett Syndrome, Breeding limitations, Actively breeding colony
Startle Prepulse Inhibition *	Risperidone	Sensorimotor gating	Mouse	Short lead time required, Good reproducibility, Group sizes n>10

Neurophysiology:

Assay	Validating Compound	Parameters	Species	Comments
C-fiber Pain Reflex Electromyography (EMG)	N/A	Flexor (C-fiber), Ia, H reflex aptitudes	Rat	Muscle response, spasticity Highly specialized capability
Cortical EEG Frequency	N/A	Cortical EEG activity evaluated as function of frequency	Mouse, Rat	Highly specialized capability
Cortical Sensory Evoked Potentials	N/A	Cortical response to peripheral sensory stimulus	Rat	Cognitive disorders (Schizophrenia, Stroke, Head Injury), Highly specialized capability
EEG Sleep/Wake and Motor Activity	Caffeine, Modafinil, Pentobarbital	Sleep architecture, Circadian rhythm, Sleep/wake enhancement, CNS drug side-effects	Mouse, Rat	Highly specialized capability
Motor Evoked Potentials and Nerve Conduction	N/A	Nerve conduction velocity, Neuromuscular function	Rat	ALS, Motor Neuron Diseases, Highly specialized capability
Proprioceptive Spinal Reflexes	N/A	H/M response amplitude	Rat	Highly specialized capability
Pro- and Anti-Convulsant Evaluation	Diazepam, Pentylentetrazol	Sub-clinical seizure threshold in response to seizure-inducing agents	Mouse, Rat	Highly specialized capability
Subthalamic Nucleus (STN) Recording <i>in vivo</i>	N/A	STN bursting patterns	Rat	Neurodegenerative model of Parkinson's Disease, Highly specialized capability

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Pain:

Assay	Validating Compound	Parameters	Species	Comments
Acetylcholine Writhing *	Morphine	Time to onset of writhing, Number of writhes	Mouse	Short lead time required, Good reproducibility
Capsaicin Hyperalgesia Assay	Morphine	Pain responsiveness after capsaicin inflammation	Rat	Short lead time, Good reproducibility
Chemotherapy-Induced Neuropathy	Morphine	Pain response after chemotherapy	Rat	In development
Chronic Constrictive Injury	Gabapentin	Pain responsiveness after sciatic constriction	Mouse, Rat	Surgically complex and specialized, Chronic model, Group sizes of n=10
Cold Response	Morphine	Latency to paw withdrawal from cold water bath	Mouse, Rat	Short lead time required, Group sizes n>10
Diabetic Neuropathy – Streptozotocin Rat Model	Streptozotocin	Development of neuropathies in STZ-treated rats	Rat	Chronic study, Specialized study
Formalin Analgesia Assay *	Oxycodone	Duration of Phase I (acute) pain, Duration of Phase II (delayed) pain	Mouse, Rat	Short lead time, Good reproducibility
Hargreaves Hyperalgesia *	Morphine	Radiant heat response	Mouse, Rat	Short lead time, Good reproducibility, Group size n>10
Hot Plate *	Morphine	Latency to pain response	Mouse, Rat	Short lead time, Good reproducibility
Migraine	Sumatriptan	Periorbital pain response after prostaglandin brain infusion	Rat	Newly developed, Highly specialized
Spinal Nerve Ligation	Gabapentin, Morphine	Paw withdrawal threshold in response to von Frey filaments	Rat	Model of neuropathic pain, Good reproducibility
Tail-Flick *	Morphine	Tail heat response, Lamp or tail immersion	Rat	Short lead time, Good reproducibility
Tail Immersion	Morphine, Oxycodone	Measures spinally-driven aspects of pain, Tail heated water bath response	Mouse	Short lead time, Good reproducibility
von Frey/Carrageenan Sensitivity *	Indomethacin	Pain responsiveness after carrageenan inflammation	Mouse, Rat	Short lead time, Good reproducibility

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Psychiatric and Cognitive:

Assay	Validating Compound	Parameters	Species	Comments
Chronic Mild Stress – Corticosterone Levels *	Desipramine	Corticosterone levels after physical and/or immunological stress, Coupled stress-induced fecal output	Mouse, Rat	Chronic study, Good reproducibility, Group sizes n>12
Chronic Mild Stress - Stress-Induced Hyperthermia *	Diazepam	Core body temperature in response to stress	Mouse, Rat	Short lead time, Good reproducibility
Chronic Mild Stress – Tail Suspension Test	Desipramine	Response in depression assay after chronic stress	Mouse, Rat	Chronic study, Good reproducibility
Elevated Plus Maze	Diazepam	Time in open vs. closed arms	Mouse, Rat	Short lead time required, Good reproducibility, Group sizes n>10
Fear Conditioning	Rolipram	Contextual memory	Mouse	Newly developed, Group sizes n>10
Forced Swim Test *	Imipramine	Duration of behavioral despair	Mouse	Short lead time required, Good reproducibility, Group size n>8
Light Dark Transitions *	Diazepam	Ratio in time in light and dark spaces	Mouse	Newly developed, Group sizes n>10
Morris Water Maze	Scopolamine	Visual spatial navigation	Mouse, Rat	Short lead time required, Good reproducibility
Novel Object Recognition Test	Scopolamine	Cognition, Recognition index	Mouse, Rat	Inter-experiment variability
Open-field Activity *	Risperidone	Locomotor parameters in an automated open-field	Mouse, Rat	Typically coupled with other assays, Short lead time required, Good reproducibility
Rotarod *	Haloperidol	Coordination, Acceleration	Mouse, Rat	Primarily utilized as pharmacology safety assay
Social Recognition	Armodafinil	Short term memory, Investigation duration	Rat	Short lead time required, Good reproducibility
Startle Prepulse Inhibition *	Risperidone	Sensorimotor gating	Mouse	Short lead time required, Good reproducibility, Group sizes n>10
Stress-Induced Fecal Production *	N/A	Fecal counts after restraint stress, Coupled with corticosterone levels	Mouse, Rat	Short lead time required, Good reproducibility
Tail Suspension *	Desipramine	Duration of behavioral despair	Mouse	Short lead time required, Good reproducibility, Group size n>10
Telemetry: Home Cage Activity	N/A	Multiple home cage activities, Locomotion, Core body temperature	Mouse, Rat	Fast turn-around, Typically coupled with other assays
Vogel Water Conflict	Diazepam	Avoidance behavior to shock	Rat	Newly developed, Group sizes n>10

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Pulmonary:

Assay	Validating Compound	Parameters	Species	Comments
LPS – Pulmonary Inflammation *	Dexamethasone	Cytokine and MCP-1 levels in dissected lung tissue, Cellular infiltrate analysis	Mouse, Rat	Acute model, Short lead time required, Good reproducibility
Pulmonary Allergic Asthma*	Dexamethasone	Cytokine and MCP-1 levels in dissected lung tissue, Cellular infiltrate analysis	Mouse, Rat	<i>Ovalbumin</i> Chronic Model, Short lead time required, Good reproducibility
Respiratory Depression	Morphine	Pulse Oximetry (O2 saturation)	Mouse, Rat	Short lead time required, Good reproducibility

Tissue Repair:

Assay	Validating Compound	Parameters	Species	Comments
Liver Fibrosis	N/A	Hydroxyproline, AST, and ALT levels after CCL4 treatment	Mouse	Short lead time required, No positive control available
Pulmonary Fibrosis	Nintedanib	Hydroxyproline levels and lung function after bleomycin treatment	Mouse	Short lead time required
Wound Healing *	N/A	Latency to heal after 8mm skin biopsy punch	Mouse, Rat	Short lead time required, No positive control available

Urogenital:

Assay	Validating Compound	Parameters	Species	Comments
Micturition, Overactive Bladder, Urinary Incontinence	Oxybutynin	Urinary latency, frequency, and volume	Mouse, Rat	Short lead time required, Good reproducibility

Drug Abuse and Addiction:

Assay	Validating Compound	Parameters	Species	Comments
Conditioned Place Preference	Morphine, Oxycodone, (-) Pentazocine	Preference Score (seconds)	Mouse, Rat	Variable duration depending upon training paradigm selected
Drug Discrimination	Amphetamine	Response rate (lever press)	Mouse, Rat	Variable duration depending upon training paradigm selected
Locomotor Sensitization	Amphetamine, Nicotine/Varenicline	Locomotor activity following drug administration over a 2-week period	Mouse, Rat	An early indicator of abuse liability
Self-Administration	Morphine	Rate of self-administration events following a training period	Mouse, Rat	A gold standard model of abuse potential, Longer duration required for training paradigm
Withdrawal/Dependence	N/A	Withdrawal syndrome (teeth chatter, yawns, shakes/tremors, abdominal writhes/gasps), Changes in systolic/diastolic blood pressure, heart rate	Mouse, Rat	Can be combined with Irwin assay

General Safety Assessment:

Assay	Validating Compound	Parameters	Species	Comments
Histology	N/A	Histology evaluation, immunohistochemistry staining, pathology scoring, cell counting, FACS analysis	Mouse, Rat	Histology services in collaboration with CaresBio Laboratory
Irwin *	Diazepam	Clinical evaluation of neurobiological and physiological parameters	Mouse, Rat	Can be used as safety pharmacology assay or to interpret other responses
Open-Field Activity *	Risperidone	Locomotor parameters in an automated open field	Mouse, Rat	Typically coupled with other assays, Short lead time required, Good reproducibility
Pharmacokinetics	N/A	Volume of distribution, half-life, total drug exposure, clearance, oral bioavailability and Cmax, trough drug plasma levels	Mouse, Rat	Useful for drug exposure, pharmacokinetic modelling, prediction of dose requirements, assess bioavailability/bioequivalence
Rotarod *	Haloperidol	Coordination, Acceleration	Mouse, Rat	Primarily utilized as pharmacology safety assay

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Pharmacokinetics/Pharmacodynamics:

Assay	Validating Compound	Parameters	Species	Comments
Bioanalysis	N/A	Small molecule concentrations	Mouse, Rat	Bioanalysis services in collaboration with Keystone Bioanalytical
Pharmacokinetics	N/A	Volume of distribution, half-life, total drug exposure, clearance, oral bioavailability and Cmax, trough drug plasma levels	Mouse, Rat	Useful for drug exposure, pharmacokinetic modelling, prediction of dose requirements, assess bioavailability/bioequivalence
Receptor Occupancy	Buprenorphine, Naloxone	Interaction of drug candidates with their targets in the brain	Mouse, Rat	Typical group size: n=4

Seizure Potential:

Assay	Validating Compound	Parameters	Species	Comments
6-Hz Psychomotor Seizure	Valproate	Seizure exhibition	Mouse	Epilepsy Fast turn-around time, Good reproducibility
Audiogenic Seizure/FMR1 Knockout	R-baclofen	Locomotor activity, Seizure (score 0-4)	Mouse	Fragile X Model Short lead time required, Good reproducibility
Lithium Pilocarpine Status Epilepticus	Diazepam, Pilocarpine	Cortical EEG activity in response to pilocarpine-induced SE	Rat	CNS/Epilepsy, Short lead time required, Good reproducibility
Pro- and Anti-Convulsant Evaluation	Diazepam, Pentylentetrazol	Sub-clinical seizure threshold in response to seizure-inducing agents	Mouse, Rat	Highly specialized capability
Pentylentetrazol-Induced Seizures *	Diazepam	Time to initial colonic seizure, Time to initial tonic seizure, EEG measurements	Mouse, Rat	CNS/Epilepsy, Short lead time required, Good reproducibility
Maximal Electroshock *	Phenytoin	Seizure (presence/absence)	Mouse	6 Hz seizure, Short lead time required, Good reproducibility

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