*thera*TRACE® Platform Assays

Acetylcholine Writhing
Bleed Time
Blood Analysis
Catalepsy
Chronic Contact Sensitivty
Chronic Mild Stress – Corticosterone Levels
Clinical Chemistries
Collagen Induced Arthritis
Colonic Propulsion
Contact Dermatitis
Delayed-Type Hypersensitivity
DEXA (High Fat Diet)
Diet-Induced Obesity
Experimental Autoimmune Encephalomyelitis
Fecal Accumulation
Food Intake
Forced Swim Test
Formalin Analgesia Assay
Gastrointestinal Transit
Grip Strength
Hargreaves
Hot Plate Analgesia Assay
Insulin Tolerance Test (ITT)
Irwin
Light Dark Transitions
LPS- Pulmonary Inflammation
LPS- Systemic Inflammation
Maximal Electroshock
Metabolic Hormone Levels
Micturition – Diuretic-Induced Stress
Monocyte Infiltration
Morphine-Induced Constipation
MPTP-Induced Parkinson's Disease
Open-Field Activity
Oral Glucose Tolerance Test (OGTT)
Pentylenetetrazole-Induced Seizures
Pulmonary Inflammation
Sebum Production
Startle-Prepulse Inhibition
Stress-Induced Fecal Production
Stress-Induced Hyperthermia
Tail Suspension
Tail-Flick
von Frey/Carrageenan Sensitivity
Weight Gain

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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	Candesartan	Blood pressure and heart rate	Rat	Short lead time required, Group size n>12
Telemetry	Candesartan	SHR Rats Blood Pressure/ MAP Heart Rate Locomotor and Open-field activity	Hamster, Mouse, Rat	Surgically complex

Fibrosis:

Assay	Validating Compound	Parameters	Species	Comments
Liver Fibrosis	N/A	TBD	Mouse	In development
Pulmonary Fibrosis	N/A	TBD	Mouse	In development
Wound Healing *	N/A	Latency to heal an 8mm skin biopsy punch	Mouse	Short lead time required, No positive control available

Gastrointestinal:

Assay	Validating Compound	Parameters	Species	Comments
Acetylcholine Writhing *	Morphine	Time to writhing onset Number of writhes	Mouse	Short lead time required, Good reproducibility
Colonic Propulsion *	Morphine	Latency to colonic expulsion of glass bead	Mouse, Rat	Short lead time required, Good reproducibility
DSS- Model of Colitis *	Cyclosporine A	Body weight Gastrointestinal distress	Mouse	Short lead time required, Good reproducibility
Fecal Accumulation *	N/A	Charcoal transit distance and time	Mouse, Rat	Short lead time required, Good reproducibility
Gastrointestinal Transit *	Morphine	Intestinal distance travelled of gavage-administered charcoal bolus	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

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Hair Growth and Dermatitis:

Assay	Validating Compound	Parameters	Species	Comments
Contact Dermatitis*	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
Chronic Contact Hypersensitivity*	Tacrolimus	Swelling of ears chronically challenged with DNFB, Clinical evaluation of ear redness, Scratching behavior in response to challenge, Cytokine/IL levels in ear biopsies, INF-γ	Mouse	Chronic model
Delayed-Type Hypersensitivity*	Dexamethasone	Footpad thickness after immunogenic challenge measured by digital caliper	Mouse, Rat	Short lead time required, Good reproducibility
Hair Growth Assay	Minoxidil	Hair growth score, Time and magnitude	Mouse	Chronic Model
Pruritus Scratching Model	U-50,488	Scratching behavior after chloroquine challenge	Mouse	Short lead time required, Good reproducibility
Sebum Production *	N/A	Sebum production, Fur water retention	Mouse	No positive control available

Inflammation and Arthritis:

Assay	Validating Compound	Parameters	Species	Comments
Capsaicin Analgesia Assay	Morphine	Pain responsiveness after capsaicin inflammation	Rat	Short lead time required, Good reproducibility
Chronic Contact Hypersensitivity *	Tacrolimus	Swelling of ears chronically challenged with DNFB, Clinical evaluation of ear redness Scratching behavior in response to challenge Cytokine/IL Levels in ear biopsies, INF- γ	Mouse	Chronic model
Collagen Induced Arthritis *	Dexamethasone	Clinical evaluation of paw and joint inflammation	Mouse, Rat	Strain Sensitive, Short lead time required, Good reproducibility

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Contact Dermatitis *	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 measured by digital caliper	Mouse, Rat	Short lead time required, Good reproducibility
Experimental Autoimmune Encephalomyelitis (EAE) *	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 Inflammation *	Dexamethasone	Cytokine and MCP-1 levels in dissected lung tissue, Cellular infiltrate analysis	Mouse, Rat	*Ovalbumin* Chronic Model, Short lead time required, Good reproducibility
von Frey/Carrageenan Sensitivity *	Indomethacin	Pain responsiveness after carrageenan inflammation	Mouse, Rat	Short lead time required, Good reproducibility
Zymosan-A Induced Peritonitis	Prednisone	Zymosan-A induces leukocyte accumulation in the peritoneum	Mouse	Short lead time required, Good reproducibility

Metabolic:

Assay	Validating Compound	Parameters	Species	Comments
Cold Sensitivity	Reserpine	Core body temperature in response to cold exposure	Mouse	Unique assay
db/db Mouse Model	Rosiglitazone	Multiple parameters: Chronic Glucose, hormones, HbA1c, pancreatic insulin, IHC	Mouse	Chronic, Good reproducibility
DEXA (High Fat Diet) *	N/A	Bone parameters and body	Mouse	Coupled with high fat diet,

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		composition (fat and lean) parameters		Good reproducibility
Diabetic Neuropathy-Streptozotocin Rat Model	N/A	Development of mechanical and thermal neuropathies in STZ-treated rats	Rat	Chronic study, Highly specialized study
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	Rosiglitazone	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
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
Stress-Induced Hyperthermia*	Diazepam	Core body temperature in response to stress	Mouse, Rat	Short lead time required, Good reproducibility

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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	Mouse, Rat	Short lead time required, Good reproducibility

Motor Function:

Assay	Validating Compound	Parameters	Species	Comments
Electromyography (EMG) C-Fiber Pain Reflex	Morphine	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
Locomotor and Open-Field Activity *	MK-801	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	Tibalis anterior and plantaris response latenties, Behavioral evaluation (limb splay, toe spread)	Mouse	ALS model Strain and supplier sensitive, Good reproducibility
Rotarod	Diazepam, Haloperidol	Coordination, Acceleration	Mouse, Rat	Primarily utilized as pharmacology safety assay

Neurology and Neurodegeneration:

Assay	Validating Compound	Parameters	Species	Comments
6 Hz Psychomotor Seizure Model	Valproate	Seizure (absence, presence)	Mouse	6 Hz seizure Short lead time, Good reproducibility
6-OHDA Lesion	Amantadine	Rotational behavior, Dopaminergic markers, Dyskinesias (AIMS, FAS)	Rat	Newly developed, Neurodegenerative symptomatic Parkinson's Disease model

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APP/PS1 Gene-Targeted Alzheimer's Disease Mouse	N/A	Aβ levels, Plaque deposition, Cognitive behavior	Mouse	Proprietary mouse model of neurodegenerative Alzheimer's disease, Well characterized Strain specific Significant lead time required
Audiogenic Seizure	Diazepam	Seizure (presence/absence)	Mouse	CNS/ Epilepsy Fragile X Syndrome Fmr1 KO mice Short lead time required, Good reproducibility
Catalepsy *	N/A	Reversal of haloperidol-induced cataleptic response	Mouse	Newly developed
Experimental Autoimmune Encephalomylitis (EAE)	FTY 720	Clinical Scores, Body weight	Mouse, Rat	Strain and supplier sensitive, Good reproducibility
FMR1; Fragile X model	Diazepam	Audiogenic seizure, Startle prepulse inhibition, Open-field activity	Mouse	Neurodegeneration/Autism Breeding limitations,
Maximal Electroshock *	Phenytoin	Seizure (absence, presence)	Mouse	60 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
Pentylenetetrazole-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, Significant lead time required
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)	Morphine	Flexor (c-fiber), Ia, H reflex amplitudes	Rat	Muscle response, spasticity Highly specialized capability

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Cortical EEG Frequency	Diazepam	EEG Power	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, Pentobarbitol	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 (SOD G93A mice), Motor Neuron Diseases, Highly specialized capability
Proprioceptive Spinal Reflexes	N/A	Stimulation of the tibial nerve resulting in M-response and H-reflex	Rat	Highly specialized capability
Pro- and Anti-Convulsant Evaluation	Diazepam, Pentylentetrazole	Sub-clinical seizure threshold in response to seizure-inducing agents	Mouse, Rat	Highly specialized capability
Status Epilepticus Model of Seizure	Diazepam	Lithium-pilocarpine induced seizures Cortical EEG recordings	Rat	Highly specialized capability

Neuropathic/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 Analgesia Assay	Morphine	Pain responsiveness after capsaicin inflammation	Rat	Short lead time, Good reproducibility
Chemotherapy-Induced Neuropathy	N/A	Pain response after chemotherapy	Rat	In development
Chronic Constrictive Injury	Gabapentin	Pain responsiveness after sciatic constriction Mechanical and thermal neuropathies	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	N/A	Development of mechanical and thermal neuropathies in STZ-treated rats	Rat	Chronic study, Specialized study

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Formalin Analgesia Assay *	Oxycodone	Duration of Phase I (acute) pain, Duration of Phase II (delayed) pain	Mouse, Rat	Short lead time required, Good reproducibility
Hargreaves *	Morphine	Radiant heat response	Mouse, Rat	Short lead time required, Good reproducibility Group size n>10
Hot Plate Analgesia Assay *	Morphine	Latency to pain response	Mouse, Rat	Short lead time required, Good reproducibility
Migraine Model	Sumatriptan	Periorbital pain response after prostaglandin brain infusion	Rat	Newly developed Highly specialized capability
Spinal Nerve Ligation Model	Gabapentin, Morphine	Paw withdrawal threshold after L5 spinal nerve ligation, Mechanical neuropathy	Rat	Newly developed Highly specialized capability
Tail-Flick *	Morphine	Tail heat response, Lamp or tail immersion	Rat	Short lead time required, Good reproducibility
Tail Immersion	Morphine	Measures spinally-driven aspects of pain, Tail heated water bath response	Mouse	Short lead time required, Good reproducibility
von Frey/Carrageenan Sensitivity *	Indomethacin	Pain responsiveness after carrageenan inflammation	Mouse, Rat	Short lead time required, Good reproducibility

Psychiatric and Cognitive:

Assay	Validating Compound	Parameters	Species	Comments
Chronic Mild Stress – Corticosterone Levels *	Desipramine Fluoxetine	Corticosterone levels after physical and/or immunological stress, Coupled stress-induced fecal output	Mouse, Rat	Chronic study, Good reproducibility
Chronic Mild Stress – Tail Suspension Test	Desipramine Fluoxetine	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 Cued fear conditioning freezing behavior	Mouse	Newly developed, Group sizes n>10 Strain specific
Forced Swim Test *	Imipramine	Duration of behavioral despair	Mouse	Short lead time required, Good reproducibility, Group size n>8
Light Dark Transitions *	Diazepam	Ratio of time in light and dark spaces Number of light dark transitions	Mouse	Newly developed, Group sizes n>10

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Novel Environment Feeding Suppression	Imipramine	Assesses stress-induced anxiety in measuring latency to eat	Mice	Group sizes n>10
Novel Object Recognition Test	Scopolamine, D-Serine	Cognition, Recognition index	Mouse, Rat	Inter-experiment variability
Open-Field Activity *	MK-801	Locomotor parameters in an automated open-field	Mouse, Rat	Typically coupled with other assays, Short lead time required Good reproducibility
Rotarod	Diazepam, other	Coordination, Acceleration	Mouse, Rat	Primarily utilized as pharmacology safety assay
Social Recognition	Armodafinil	Short-term memory difference between two inter-trial intervals Interaction between adults and familiar vs. novel juvenile rats	Rat	Specialized study
Startle Prepulse Inhibition *	Risperidone	Sensorimotor gaiting	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
Stress-induced Hyperthermia	Diazepam	Core body temperature in response to stress	Mouse, Rat	Short lead time required, Good reproducibility
Tail Suspension *	Imipramine	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

Urogenital:

Assay	Validating Compound	Parameters	Species	Comments
Micturition – Diuretic-Induced Stress *	Oxybutynin	Urinary latency, frequency, And volume	Mouse, Rat	Short lead time required, Good reproducibility

Additional information, including validation data, may be found on the Melior Discovery website.

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Drug Abuse Liability:

Assay	Validating Compound	Parameters	Species	Comments
Conditioned Place Preference	Amphetamine, Nicotine/Varenicline	Preference score (seconds)	Mouse, Rat	Variable duration depending upon training paradigm selected
Drug Discrimination	Amphetamine, Nicotine/Varenicline	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 or abuse liability
Self Administration	Amphetamine, Nicotine/Varenicline	Rate of self-administration events following a training period	Mouse, Rat	A gold standard model of abuse potential, Longer duration required for training paradigm

Seizure Potential:

Assay	Validating Compound	Parameters	Species	Comments
6 Hz Psychomotor Seizure Model	Valproate	Seizure (absence, presence)	Mouse	6 Hz seizure Good lead time, Good reproducibility
Audiogenic Seizure	Diazepam	Seizure (absence, presence)	Mouse	CNS/Epilepsy Fragile X Syndrome Model Fmr1 KO mice Short lead time required, Good reproducibility
EEG Pro- and Anti-Convulsant Evaluation	Diazepam, Pentylentetrazole	Sub-clinical seizure threshold in response to seizure-inducing agents	Mouse, Rat	Highly specialized capability
Maximal Electroshock	Phenytoin	Seizure (absence, presence)	Mouse	60 Hz seizure, Short lead time required, Good reproducibility
Pentylenetetrazole-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
Status Epilepticus Model of Seizure	Diazepam	Lithium-pilocarpine induced seizures, Cortical EEG recordings	Rat	Highly specialized capability

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General Safety Assessment:

Assay	Validating Compound	Parameters	Species	Comments
Irwin Observational Battery *	Diazepam	Clinical evaluation of neurobiological and physiological parameters	Mouse, Rat	Can be used as safety pharm assay or to interpret other responses
Open-Field Activity *	MK-801	Locomotor parameters in an automated open-field	Mouse, Rat	Typically coupled with other assays, Short lead time required Good reproducibility
Rotarod *	Diazepam, other	Coordination, Acceleration	Mouse, Rat	Primarily utilized as pharmacology safety assay

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general analyses

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General Analyses:

Assay	Validating Compound	Parameters	Species	Comments
Blood Analysis *	N/A	Standard blood differential	Mouse, Rat	Standard
Clinical Chemistries *	N/A	Standard clinical chemistries	Mouse, Rat	Standard

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