

<b>ASSAY (VALIDATING COMPOUND)</b>	<b>THERAPEUTIC AREA</b>	<b>PARAMETER</b>	<b>SPECIES</b>	<b>NUMBER OF VALIDATIONS (2 YEARS)</b>	<b>COMMENTS</b>
<b>Bleeding time assay *</b> (heparin)	Cardiovascular	<ul style="list-style-type: none"> <li>Time to bleeding cessation</li> </ul>	Rat/Mouse	6	Short lead time req'd Good reproducibility
<b>Blood Pressure Tail Cuff</b> (nifedipine)	Cardiovascular	<ul style="list-style-type: none"> <li>BP</li> <li>HR</li> </ul>	Rat	2	Short lead time req'd Group sizes of > 12
<b>Telemetry: Blood Pressure; Heart-Rate</b> (nifedipine)	Cardiovascular	<ul style="list-style-type: none"> <li>SHR rats</li> <li>BP/MAP</li> <li>HR</li> <li>Locomotion/Home Cage Activity</li> </ul>	Rat/Mouse/Hamster	6	Surgically complex
<b>EEG: seizure threshold</b> (pentylenetetrazole)	CNS	<ul style="list-style-type: none"> <li>Sub-clinical seizure threshold in response to seizure inducing agents</li> </ul>	Rat/Mouse	8	Highly specialized capability
<b>EEG: sleep wake</b> (modafinil)	CNS	<ul style="list-style-type: none"> <li>Circadian rhythm</li> <li>Sleep architecture</li> </ul>	Rat (mouse in development)	8	Highly specialized capability
<b>Audiogenic Seizure</b>	CNS/Epilepsy	<ul style="list-style-type: none"> <li>Seizure (presence/absence)</li> </ul>	Mouse	2	Short lead time req'd Good reproducibility
<b>Maximal electroshock *</b> (gabapentin)	CNS/Epilepsy	<ul style="list-style-type: none"> <li>Seizure (presence/absence)</li> </ul>	Rat/Mouse	14	Short lead time req'd Good reproducibility
<b>Pentylenetetrazole-induced Seizure *</b> (diazepam)	CNS/Epilepsy	<ul style="list-style-type: none"> <li>Time to initial clonic seizure</li> <li>Time to initial tonic seizure</li> <li>EEG measurements</li> </ul>	Rat/Mouse	14	Short lead time req'd Good reproducibility



<b>EEG: Peripheral Nerve conduction velocity</b>	CNS/PNS	<ul style="list-style-type: none"> <li>Nerve conduction velocity</li> </ul>	Rat	6	Highly specialized capability
<b>Somatosensory Evoked Potential</b>	CNS/PNS	<ul style="list-style-type: none"> <li>Electrical potential measured after peripheral stimulus</li> </ul>	Rat	2	Highly specialized capability
<b>Sebum production</b>	Dermatology	<ul style="list-style-type: none"> <li>Sebum production</li> <li>Fur water retention</li> </ul>	Mouse	2	Difficult assay No positive control response
<b>Hair Growth (Minoxidil)</b>	Dermatology / Alopecia	<ul style="list-style-type: none"> <li>Hair growth score</li> <li>Time and magnitude</li> </ul>	Mouse	6	Chronic model
<b>Colonic expulsion test * (morphine)</b>	Gastrointestinal	<ul style="list-style-type: none"> <li>Latency to colonic expulsion of a glass bead</li> </ul>	Rat/Mouse	6	Short lead time req'd Good reproducibility
<b>Fecal Accumulation *</b>	Gastrointestinal	<ul style="list-style-type: none"> <li>Charcoal transit distance and time</li> </ul>	Rat/Mouse	8	Short lead time req'd Good reproducibility
<b>Gastrointestinal Transit *</b>	Gastrointestinal	<ul style="list-style-type: none"> <li>Intestinal distance travelled of gavage-administered charcoal bolus</li> </ul>	Rat/Mouse	6	Short lead time req'd Good reproducibility
<b>Morphine-Induced Constipation * (naloxone)</b>	Gastrointestinal	<ul style="list-style-type: none"> <li>Latency of colonic expulsion of a glass bead</li> </ul>	Rat/Mouse	6	Short lead time req'd Good reproducibility
<b>DSS-induced colitis * (cyclosporine A)</b>	Gastrointestinal; IBD	<ul style="list-style-type: none"> <li>Body weight</li> <li>GI distress</li> </ul>	Mouse	8	Short lead time req'd Good reproducibility



<b>Blood analysis *</b>	General	<ul style="list-style-type: none"> <li>Standard blood differential</li> </ul>	Rat Mouse	10	Standard
<b>Clinical Chemistries *</b>	General	<ul style="list-style-type: none"> <li>Standard clinical chemistry</li> </ul>	Rat/Mouse	10	Standard
<b>Monocyte Infiltration * (dexamethasone)</b>	Inflammation	<ul style="list-style-type: none"> <li>MCP-1 levels from peritoneal lavage</li> <li>Differentials</li> </ul>	Rat/Mouse	6	Short lead time req'd Good reproducibility
<b>Pulmonary inflammation (LPS) * (dexamethasone)</b>	Inflammation / Asthma	<ul style="list-style-type: none"> <li>Cytokine and MCP-1 levels in dissected lung tissue</li> <li>Cellular Infiltrate Analysis</li> </ul>	Rat/Mouse	8	Acute model Short lead time req'd Good reproducibility
<b>Delayed Type Hypersensitivity * (dexamethasone)</b>	Inflammation, Allergy	<ul style="list-style-type: none"> <li>Footpad thickness after immunogenic challenge</li> </ul>	Rat/Mouse	10	Short lead time req'd Good reproducibility
<b>Chronic Contact Hypersensitivity * (Tacrolimus)</b>	Inflammation, Allergy; Dermatology	<ul style="list-style-type: none"> <li>Swelling of ears chronically challenged with DNFB</li> <li>Clinical evaluation of Ear Redness</li> <li>Scratching Behavior in response to challenge</li> <li>Cytokine/IL levels in Ear Biopsies, INF-<math>\gamma</math></li> </ul>	Mouse	4	Chronic Model
<b>Contact Dermatitis * (dexamethasone)</b>	Inflammation, Allergy; Dermatology	<ul style="list-style-type: none"> <li>Swelling of ears sensitized to oxazolone, PPD or DNFB</li> <li>Clinical evaluation of Ear Redness</li> <li>Cytokine/IL levels in Ear Biopsies, INF-<math>\gamma</math></li> </ul>	Rat/Mouse	10	Short lead time req'd Good reproducibility
<b>Collagen-induced arthritis * (dexamethasone)</b>	Inflammation/Arthritis	<ul style="list-style-type: none"> <li>Clinical evaluation of paw and joint inflammation</li> </ul>	Rat/Mouse	6	Strain sensitive Strain sensitive Short lead time req'd Good reproducibility
<b>Pulmonary inflammation (ovalbumen) * (dexamethasone)</b>	Inflammation/Asthma	<ul style="list-style-type: none"> <li>Cytokine and MCP-1 levels in dissected lung tissue</li> <li>Cellular Infiltrate Analysis</li> </ul>	Rat/Mouse	4	Chronic model Short lead time req'd Good reproducibility



<b>Experimental Autoimmune Encephalomyelitis *</b> (cyclosporine A)	Inflammation/CNS	<ul style="list-style-type: none"> <li>Clinical Scores</li> <li>Body weight</li> </ul>	Rat/Mouse	6	Strain and supplier sensitive; Good reproducibility
<b>LPS-Induced Systemic Inflammation *</b> (dexamethasone)	Inflammation/Sepsis	<ul style="list-style-type: none"> <li>TNF<math>\alpha</math> and IL-6 blood levels after Lipopolysaccharide challenge</li> </ul>	Rat/Mouse	14	Acute model Short lead time req'd Good reproducibility
<b>Cold-sensitivity (reserpine)</b>	Metabolic	<ul style="list-style-type: none"> <li>Core body temperature in response to cold exposure</li> </ul>	Mouse	2	Unique assay
<b>Glucose Clamp</b>	Metabolic	<ul style="list-style-type: none"> <li>Hyperinsulinemic euglycemic clamp</li> <li>Glucose infusion rate to maintain euglycemia with constant insulin infusion rate</li> <li></li> </ul>	Rat / Mouse	2	Gold standard measure of insulin sensitivity
<b>DEXA *</b> (High Fat Diet)	Metabolic	<ul style="list-style-type: none"> <li>Bone parameters and body composition (fat and lean) parameters</li> </ul>	Mouse	6	Coupled with high fat diet Good reproducibility
<b>Metabolic hormone levels *</b>	Metabolic	<ul style="list-style-type: none"> <li>Leptin, insulin adiponectin, c-peptide etc in response to multiple challenges (high fat diet, drug treatment, acute/chronic)</li> </ul>	Rat/Mouse	12	Coupled with multiple metabolic assays Short lead time req'd Good reproducibility
<b>Standard Diet Food Intake *</b> (imipramine)	Metabolic	<ul style="list-style-type: none"> <li>Quantity of food ingested per day and per gram of body weight</li> <li>Food ingested after fasting</li> </ul>	Rat/Mouse	10	Short lead time req'd Good reproducibility
<b>Standard Diet Weight Gain *</b> (imipramine)	Metabolic	<ul style="list-style-type: none"> <li>Weight change from initial measurement</li> <li>Weight change per day</li> </ul>	Rat/Mouse	10	Short lead time req'd Good reproducibility
<b>Standard Diet Weight Gain *</b> (imipramine)	Metabolic	<ul style="list-style-type: none"> <li>Weight change from initial measurement</li> <li>Weight change per day</li> </ul>	Rat/Mouse	10	Short lead time req'd Good reproducibility



<b>Stress-induced hyperthermia</b>	Metabolic	<ul style="list-style-type: none"> <li>Core body temperature in response to stress</li> </ul>	Mouse/Rat	4	Short lead time req'd Good reproducibility
<b>ZDF rats (insulin)</b>	Metabolic	<ul style="list-style-type: none"> <li>Multiple parameters</li> <li>Chronic glucose, hormones, HbA1c, pancreatic insulin IHC</li> </ul>	Rat	6	Highly specialized Supplier sensitivity
<b>Streptozotocin-induced Diabetes (Insulin)</b>	Metabolic / Type 1 diabetes	<ul style="list-style-type: none"> <li>Multiple parameters</li> <li>Chronic glucose, hormones, HbA1c</li> <li>Diuresis and Nephropathy</li> </ul>	Mouse / Rat	4	Highly specialized Well-characterized
<b>Db/db mouse * (rosiglitazone)</b>	Metabolic/Diabetes	<ul style="list-style-type: none"> <li>Multiple parameters</li> <li>Chronic glucose</li> <li>Hormones</li> <li>HbA1c</li> <li>pancreatic insulin</li> <li>IHC</li> </ul>	Mouse	6	Chronic Good reproducibility
<b>Insulin tolerance test * (insulin)</b>	Metabolic/Diabetes	<ul style="list-style-type: none"> <li>Glucose response to insulin</li> </ul>	Rat/Mouse	18	Short lead time req'd Good reproducibility
<b>Ob/ob mouse (rosiglitazone)</b>	Metabolic/Diabetes	<ul style="list-style-type: none"> <li>Multiple parameters</li> <li>Chronic glucose, hormones, HbA1c, pancreatic insulin IHC</li> </ul>	Mouse	6	Chronic- Good reproducibility
<b>Oral glucose tolerance test * (metformin)</b>	Metabolic/Diabetes	<ul style="list-style-type: none"> <li>Glucose levels over a trial period after glucose challenge</li> <li>Prior and after high fat diet regimen</li> </ul>	Rat/Mouse	40	Short lead time req'd Good reproducibility Can be coupled with high fat diet model
<b>High Fat (Western) Diet * (imipramine)</b>	Metabolic/obesity-metabolic syndrome	<ul style="list-style-type: none"> <li>Quantity of food ingested per day and per gram of body weight</li> <li>Weight change over time</li> <li>Weight change from initial measurement</li> </ul>	Rat/Mouse	8	Short lead time req'd Good reproducibility
<b>Irwin's Battery of Tests * (diazepam)</b>	Multiple	<ul style="list-style-type: none"> <li>Clinical evaluation of neurobiological and physiological parameters</li> </ul>	Rat/Mouse	20	Can be used as safety pharm assay or to interpret other responses



<b>Open Field Locomotor Activity * (diazepam)</b>	Multiple	<ul style="list-style-type: none"> <li>• Locomotor parameters in an automated open-field</li> </ul>	Rat/Mouse	18	Short lead time req'd Good reproducibility Typically coupled with other assays
<b>Rotarod (ethanol)</b>	Multiple	<ul style="list-style-type: none"> <li>• Coordination</li> <li>• Accelerating</li> </ul>	Rat Mouse	10	Used mostly as safety pharm assay
<b>Telemetry: Home-Cage Activity</b>	Multiple	<ul style="list-style-type: none"> <li>• Multiple home cage activities</li> <li>• Locomotion</li> <li>• Core body temperature</li> </ul>	Rat/Mouse	4	Fast-turn-around Typically coupled with other assays
<b>Electromyography</b>	Muscle response; pain	<ul style="list-style-type: none"> <li>• Flexor reflex</li> </ul>	Rat	6	Highly specialized capability
<b>FMR1; Fragile X model</b>	Neurodegeneration / Fragile X; Autism	<ul style="list-style-type: none"> <li>• Audiogenic seizure</li> <li>• Startle prepulse inhibition</li> <li>• Open-field activity</li> </ul>	Mouse	6	Breeding limitations Active breeding colony
<b>Rett Syndrome Neurodevelopment Model</b>	Neurodegeneration / Rett syndrome	<ul style="list-style-type: none"> <li>• Locomotor</li> <li>• Respiration</li> <li>• Seizure</li> <li>• Mortality</li> </ul>	Mouse	8	Breeding limitations Actively breeding colony
<b>6-OHDA lesion (l-dopa)</b>	Neurodegeneration; Parkinson's disease	<ul style="list-style-type: none"> <li>• Rotational behavior</li> <li>• Dopaminergic markers</li> <li>• Dyskinesias</li> </ul>	Rat/Mouse	-	Newly developed Symptomatic Parkinson's disease model
<b>MPTP-induced Parkinson's * (l-deprenyl)</b>	Neurodegeneration: Parkinson's disease	<ul style="list-style-type: none"> <li>• Locomotor parameters in an automated open-field apparatus</li> <li>• Brain (striatal) dopamine levels</li> <li>• Dopamine cell number (TH staining; substantia nigra)</li> </ul>	Mouse	12	Strain and supplier sensitive Short lead time req'd Good reproducibility



<b>APP/PS1 Gene Targeted Alzheimer's disease mouse</b>	Neurodegeneration/Alzheimer's disease	<ul style="list-style-type: none"> <li>• A<math>\beta</math> levels</li> <li>• Plaque deposition</li> <li>• Cognitive behavior</li> </ul>	Mouse	6	Proprietary mouse model of AD Active breeding colony Well-characterized
<b>Formalin test * (oxycodone)</b>	Pain; chemical	<ul style="list-style-type: none"> <li>• Duration of Phase I (acute) pain</li> <li>• Duration of Phase II (delayed) pain</li> </ul>	Rat/Mouse	12	Short lead time req'd Good reproducibility
<b>Chemotherapy-induced neuropathy</b>	Pain; neuropathic	<ul style="list-style-type: none"> <li>• Pain response after chemotherapy</li> </ul>	Rat	-	In development
<b>Hargreaves * (morphine)</b>	Pain; thermal	<ul style="list-style-type: none"> <li>• Radiant heat response</li> </ul>	Rat/Mouse	10	Short lead time req'd Good reproducibility Group sizes of > 10
<b>Hot plate * (oxycodone)</b>	Pain; thermal	<ul style="list-style-type: none"> <li>• Latency to pain response</li> </ul>	Rat/Mouse	20	Short lead time req'd Good reproducibility
<b>Tail-flick (morphine)</b>	Pain; thermal	<ul style="list-style-type: none"> <li>• Tail heat response</li> <li>• Lamp or tail immersion</li> </ul>	Rat/Mouse	12	Short lead time req'd Good reproducibility
<b>Acetylcholine Writhing * (morphine)</b>	Pain/ Gastrointestinal	<ul style="list-style-type: none"> <li>• Time to onset of writhing</li> <li>• Number of writhes</li> </ul>	Mouse	6	Short lead time req'd Good reproducibility
<b>Von Frey with Carrageenan Challenge * (indomethacin)</b>	Pain/Inflammation	<ul style="list-style-type: none"> <li>• Pain responsiveness after carrageenan inflammation</li> </ul>	Rat/Mouse	12	Short lead time req'd Good reproducibility
<b>Chronic Constrictive Injury; Chung Model (gabapentin)</b>	Pain/Neuropathic	<ul style="list-style-type: none"> <li>• Pain responsiveness after sciatic constriction</li> </ul>	Rat/Mouse	4	Surgically complex and specialized; chronic model Group sizes of 10 recommended



<b>Light / Dark Transitions (diazepam)</b>	Psychotherapeuti/anxiety	<ul style="list-style-type: none"> <li>Ratio of time in light and dark spaces</li> </ul>	Mouse	1	Newly developed Group sizes of >10
<b>Stress-induced corticosterone levels *</b>	Psychotherapeutic / Anxiety	<ul style="list-style-type: none"> <li>Corticosterone levels after physical and/or immunological stress</li> <li>Coupled stress-induced fecal output</li> </ul>	Rat /Mouse	6	Short lead time req'd Good reproducibility
<b>Stress-induced Fecal Production *</b>	Psychotherapeutic / Anxiety	<ul style="list-style-type: none"> <li>Fecal counts after restraint stress</li> <li>Coupled with corticosterone levels</li> </ul>	Rat/Mouse	6	Short lead time req'd Good reproducibility
<b>Forced Swim * (imipramine)</b>	Psychotherapeutic / Depression	<ul style="list-style-type: none"> <li>Duration of behavioral despair over trial</li> </ul>	Mouse	12	Short lead time req'd Good reproducibility Group sizes of >8
<b>Tail Suspension * (imipramine)</b>	Psychotherapeutic / Depression	<ul style="list-style-type: none"> <li>Duration of behavioral despair over trial</li> </ul>	Mouse	12	Short lead time req'd Good reproducibility Groups sizes of >10
<b>Novel Object Recognition (scopolamine)</b>	Psychotherapeutic/ cognition	<ul style="list-style-type: none"> <li>Cognition</li> <li>Recognition Index</li> </ul>	Rat/Mouse	2	Interexperiment variability
<b>Startle Prepulse Inhibition (haloperidol)</b>	Psychotherapeutic/ Schizophreniz	<ul style="list-style-type: none"> <li>Sensorimotor gating</li> </ul>	Mouse	6	Short lead time req'd Good reproducibility Groups sizes of >10
<b>Elevated Plus Maze (diazepam)</b>	Psychotherapeutic/Anxiety	<ul style="list-style-type: none"> <li>Time in open vs closed arms</li> </ul>	Rat/Mouse	6	Short lead time req'd Good reproducibility Group sizes of >10
<b>Vogel Water Conflict (diazepam)</b>	Psychotherapeutic/Anxiety	<ul style="list-style-type: none"> <li>Avoidance behavior to shock</li> </ul>	Rat	-	Newly developed Group sizes of >10



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<b>Chronic Mild Stress (fluoxetine)</b>	Psychotherapeutic/chronic depression	<ul style="list-style-type: none"><li>• Response in depression assays after chronic stress</li></ul>	Mouse	2	Newly developed
<b>Fear Conditioning (rolipram)</b>	Psychotherapeutic/cognition	<ul style="list-style-type: none"><li>• Contextual memory</li></ul>	Mouse	1	Newly developed Group sizes of >10
<b>Diuretic Induced Stress (Micturition) * (oxybutynin)</b>	Urogenital	<ul style="list-style-type: none"><li>• Urinary latency</li><li>• Urinary frequency over trial</li><li>• Urinary volume over trial</li></ul>	Rat/Mouse	4	Short lead time req'd Good reproducibility

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Indicates models that can be included in *theraTRACE*<sup>®</sup> platform