



ALTASCIENCES

PAIN MODELS

Altasciences has over two decades of experience in the design and conduct of clinical pharmacology studies on pain medications. Pain models can be an important translational tool in characterizing the analgesic action of a novel drug early in clinical development.

Our pain experts and neuroscientists can assist you in selecting the most appropriate pain model to successfully evaluate the efficacy and safety profile of your study drug, consulting with other key opinion leaders as needed.

Our Team

- Our core team includes central nervous system (CNS) experts in anesthesiology, pain management, neuropsychology, clinical pharmacology, and psychiatry.
- We employ the services of Cambridge Cognition and Medoc Advanced Medical Systems, two organizations with expert capabilities in the field of CNS testing.
- We collaborate with a highly experienced knee surgeon for study setup and endpoint evaluation.

Experience

- Broad range of clinical pharmacology studies on novel opioid and non-opioid analgesic drugs, including:
 - Proof of concept
 - FIH—single and multiple ascending dose
 - Opioid blockade (antagonist)
- Phase II dose-ranging studies of safety and efficacy

Patient Access

- 800+ patients with chronic pain disorders
- Lead recruitment and enrollment site for patients with osteoarthritis of the knee
- Easy access to healthy subjects through combined database of over 400,000 participants

Clinical Expertise

- Significant expertise in the evaluation of pharmacodynamic drug effects, including pain assessments
- Expert project management for multi-site trials, including training sites on recruitment and/or pain models to achieve high inter-rater agreement
- Complex and adaptive study designs, including enrichment phases to control for variability in outcome measures
- In-depth knowledge of ACTION and IMPACT

Case Studies

- [A Randomized, Controlled, Proof-of-Concept Trial in Patients with Osteoarthritis Knee Pain](#)
- [Study on Analgesia on Visceral Pain, Rectal Sensory Threshold Using the Barostat Method](#)
- [A Proof-of-Concept Study Assessing NEO6860 in Osteoarthritis Pain](#)



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ABOUT OUR PAIN MODELS

Thermal Pain Models

Cold Pressor Test

- Measures pain tolerance and cardiovascular effects when hand is submerged in cold water
- First detection of pain/subsequent withdrawal of hand measured in time, along with degree of pain, using a subjective pain scale
- Can be accompanied by an objective reading on blood pressure
 - Normally causes a reflexive increase in both heart rate and blood pressure by activating sympathetic nervous system
- Has been used to evaluate novel analgesics and diagnose/monitor certain pain conditions

Cutaneous Freeze Injury

- Involves the application of cold temperatures at a standardized pressure
- Provides stable testing conditions lasting about a day
- Manifests a local primary hyperalgesia where the application of the freeze injury was applied with secondary hyperalgesia in the surrounding area
- Sensitivity can be examined by the use of probes (e.g., von Frey) to test for hyperalgesia

UVB Hyperalgesia

- Uses irradiation with ultraviolet B, resulting in injury invoking an inflammatory response
- Simulates a condition akin to that of sunburn
- Assesses inflammatory pain
- Produces stable areas of primary hyperalgesia that can be tested over the course of several hours
- Frequently used to test analgesics

Thermal Probe

- Quantifies thermal thresholds by measuring the temperature at which withdrawal occurs

Chemical Stimulation Models

Capsaicin

- An alkaloid found in peppers
- Induces intense burning sensations
- Has agonist effect on transient receptor potential vanilloid-1 (TRPV1) ion channel receptor
 - Surrogate model inducing secondary hyperalgesia
- Applied topically (with a heat sensitization procedure) or via intra-dermal injection representing central sensitization

Electrical Stimulation Models

Transcutaneous Electrical Nerve Stimulation (TENS)

- Uses an electrical stimulator, applied to either the skin surface or intracutaneous tissue
- Delivers varying stimulation patterns with different frequencies, durations, and waveforms, which excites nerve fibers
- Can be used as a pain model to invoke a painful stimulus
 - Conversely, used to treat pain

Mechanical Stimulation Models

- Can be applied to skin, muscle, or viscera to invoke pain by touch, pin prick, pinching, application of pressure, or distention

Barostat Model (for Visceral Pain)

- A mechanical model involving distention of the viscera by the use of a balloon
- Uses a computerized air pump to measure visceral tone, compliance, and sensation of hollow organs such as the stomach or intestine
- Implementation involves intubation of esophagus to advance an infinitely compliant polyethylene balloon in the fundus
- System maintains a constant pressure and can detect changes in tone due to gastric relaxation or contraction
- Can also be used to induce pain by distention

Von Frey (Manual/Electric)

- Mechanical stimulation model that applies light pressure to assess sensitivity to touch
- Can be used to detect the effect of a local anesthetic applied directly to the skin, or in combination with other models to assess hyperalgesia in the treated and peripheral regions of the skin
- Manual and electronic versions
 - Electronic: direct readings of pressure applied

Staircase Challenge

- Useful for increasing the sensitivity of assessing analgesic effects, particularly when used in patients with osteoarthritis of the knee
- Participants must fully step on eight-inch-high (20 cm) platform with one foot then the other, and back down
 - Lead leg alternated at each up/down cycle
 - 24 repetitions
- Pain intensity assessed immediately before and after the exercise using numeric pain rating scale
- Can also be used as a muscle stimulation model to evoke pain by exercise, with delayed onset muscle soreness

Skin Punch

- Frequently used for biopsies to diagnose various conditions involving the skin and hair
- Can also be used to assess pain and wound healing in a clinical setting to test pain interventions

Additional pain models can be implemented upon request.