Pain Model Breakout Session Deliverables

1. **Representative Clinical Syndrome(s).**
   Common clinical syndromes associated with pain diagnosis (e.g., polyneuropathy: CIPN, diabetes, etc.)

2. **For your pain type/bucket, which models or ‘pain assays’ did you consider as mechanistically relevant toward assessing the effects of a therapeutic intervention?**
   Models can span the range of evoked and non-evoked pain as well as affect. Model aspects important to define include:
   i) Species
   ii) Strain
   iii) Sex
   iv) Model construct/pain-inducing insult (spinal nerve ligation, intraplantar formalin, etc.)
   v) Stimulus (tactile, thermal, spontaneous behavior, etc.)
   vi) Endpoint(s) measured (escape latency, threshold, number of flinches/time of flinching, weight bearing, CPP, marble burying, grimace, etc.)
   vii) Minimum endpoint criterion response (biologically/behaviorally relevant vs. statistically significant)
   viii) Standard drug(s) considered to have efficacy in the model (positive drug control) and/or in the patient.
   ix) Inactive drug(s) (negative drug control)

3. **Rank-order the prioritized models/pain assays based on your discussions of relative strengths and weaknesses.**
   a) Components contributing to the perceived strength of the model might include, but not limited to:
      i. Face and/or construct validity (e.g., thermal injury of paw = burn patient)
      ii. Robust and reproducible reversal of pain behaviors by positive control drugs
      iii. Baseline differential pre/post-injury (signal window between untreated and full reversal)
      iv. Ease of model creation/performance (consider training, complication of model creation (surgery, implants, etc., or not applicable)
      v. High throughput (low, medium, high, or not applicable)
   b) If your list contains more than one model/pain assay, would you recommend running only the highest ranked model or more than one?

4. **For your prioritized models/pain assays, which assays of side-effects would you consider towards establishing:**
   a) Therapeutic ratio based on changes in:
      i. Motor coordination (rotarod, etc.)
      ii. Sedation (24 hr activity, etc.)
      iii. Affect (marble burying, open field, etc.)
      iv. Physiologic parameters (cardiovascular, GI, etc.)
      v. Abuse potential (CPP, self-administration, etc.)
      vi. What fold-separation from efficacy would you consider satisfactory compared to control, whether negative or in comparison to a positive control?

5. **General questions relevant to your bucket.**
   a) Are rodent models adequate, or are models in other species and/or large animals (pig, dog, etc.) important to consider and why?
   b) What are the perceived gaps (face or construct but NOT predictive validity) in the currently available models?
   c) Is there a need to develop new models to address a particular indication, whether indications commonly studied in clinical trials such as DPNP and cancer pain or others that have received less attention such as fibromyalgia, CRPS and sickle cell disease?