INITIATIVE ON METHODS, MEASUREMENT, AND PAIN ASSESSMENT IN CLINICAL TRIALS

IMMPACT-VI (REVISED TO IMMPACT-VII)

"RANDOMIZED CLINICAL TRIALS FOR CHRONIC PAIN TREATMENTS: PLACEBO-CONTROLLED DESIGNS AND THEIR ALTERNATIVES"

June 8-10, 2006
Ritz Carlton Pentagon City
Arlington, Virginia

Thursday, June 8

7:00 PM	**RECEPTION AND DINNER** at the Ritz Carlton

Friday, June 9

7:00–8:00 AM	**CONTINENTAL BREAKFAST**
8:00–8:30 AM	**Welcome, introductions, update, objectives** Dennis Turk, PhD
8:30–9:00 AM	**Epilepsy clinical trials: state-of-the science, with focus on add-on designs** Jacqueline French, MD
9:00–9:30 AM	**Depression clinical trials: state-of-the science, with focus on placebo group response** Michael Thase, MD
9:30–10:00 AM	**Analyzing and interpreting onset of effect, durability of effect, and time to exit in clinical trials** Susan Ellenberg, PhD
10:00–10:30 AM	**COFFEE BREAK**
10:30–11:00 AM	**1. The Phase III chronic pain clinical trial** **2. Establishing an IMMPACT "Resource for Evaluating Procedures and Outcomes of Randomized Trials" (REPORT)** Bob Dworkin, PhD
11:00 AM –12:30 PM	**Study populations** moderator: Dennis Turk, PhD 1. General considerations, for example

- identifying best clinical condition(s) for a particular treatment, for example, relatively homogeneous conditions (e.g., diabetic neuropathy) vs. heterogeneous groups of patients (e.g., neuropathic pain)
- difficulties of studying neglected clinical conditions

2. Specific inclusion and exclusion criteria, for example
   - minimum baseline pain (e.g., ≥ 4/10, ≥ 5/10, ≥ 3/10)
   - can patients be trained to rate pain with greater reliability and validity?
   - minimum pain duration (e.g., ≥ 3 mos, ≥ 6 mos)
   - excluding patients refractory to multiple prior treatments
3. *How can IMMPACT interrogate existing data and generate new data?*

12:30–1:30 PM **LUNCH**

1:30–3:00 PM **Types of controlled superiority trials**
moderator: John Farrar, MD, PhD

1. Investigational treatment
   - single vs. multiple fixed dosages
   - identifying non-effective and maximum dosages
2. Placebo
   - no other treatments allowed
   - rescue allowed (e.g., acetaminophen)
   - add-on designs (e.g., pre-specified vs. any stable regimen)
3. Active comparator
4. Both of the above comparison groups
5. Studying combination therapy
6. Situations in which a non-inferiority trial would be informative
7. Randomization
   - equal allocation vs. fewer patients randomized to placebo
8. *How can IMMPACT interrogate existing data and generate new data?*

3:00–3:30 PM **COFFEE BREAK**

3:30–5:00 PM **Trial components and duration**
moderator: Bob Dworkin, PhD

1. Run-in periods
   - identifying placebo responders
   - identifying treatment responders
   - identifying poor treatment tolerability

- identifying poor adherence

2. Titration phase
3. Taper phase
4. Overall trial duration
5. Placebo group
   - anatomy of placebo group response: placebo effect, regression to the mean, natural history
   - estimating placebo group response
   - attenuating placebo group response
   - inert vs. active placebo
6. Methods to improve subject retention
7. *How can IMMPACT interrogate existing data and generate new data?*

6:45 PM **Meet in hotel lobby for transport to dinner**

7:00–9:30 PM **RECEPTION AND DINNER**

Saturday, June 10

7:00–8:00 AM **CONTINENTAL BREAKFAST**

8:00–9:30 AM **Situations that require alternative designs for Phase III clinical trials**

moderator: Dennis Turk, PhD

1. Treatments
   - opioid analgesics
   - disease modifying agents
   - prevention of chronic pain
   - others?
2. Conditions
   - osteoarthritis
   - rheumatoid arthritis
   - low back pain
   - fibromyalgia
   - visceral pain
   - others?

9:30–10:00 AM **COFFEE BREAK**

10:00–12:00 PM **Alternative designs for Phase III clinical trials**

moderator: Nat Katz, MD

1. Randomized withdrawal
2. Enriched enrollment
3. Flexible dosing
4. Crossover designs
5. Superiority
6. Adaptive allocation and Bayesian approaches
7. Others?

12:00–1:00 PM	**LUNCH**
1:00–2:30 PM	**How will IMMPACT interrogate existing data?** **How can IMMPACT generate new data?** moderator: Bob Dworkin 1. Action plan for coming year
2:30–3:00 PM	**COFFEE BREAK**
3:00–4:30 PM	**How will IMMPACT interrogate existing data?** **How can IMMPACT generate new data?** moderator: Bob Dworkin 1. Action plan for coming year 2. Identify members of implementation team
4:30 PM	**ADJOURN**