Inisights and Expertise in Labeling Comprehension and Observational Research Studies

October 2010
Core Consulting Areas:

- **Clinmetric™ Research** services:
  - Observational research studies
  - Labeling comprehension studies
    - Patient package inserts
    - Medication Guides
    - Instructional aids
    - Educational materials
  - Product usability studies
    - User acceptance
    - Comprehension and performance
    - Human factors

- **PharmaTrak™ Research** services:
  - REMS assessments for measuring the effectiveness of
    - Medication Guides
    - HCP communications
    - Other educational materials designed to mitigate risk
• Founded in 1999 to provide commercial support and new product planning consulting services to the pharmaceutical and medical device industry

• Team of 10 including researchers, Pharmacists, regulatory, biostatistics experts, and support staff based in Carlsbad, California

• Leadership from the pharmaceutical industry

• Conducted over 275 total research studies and over 50 web-based questionnaire survey studies with patients, health care providers, and pharmacists

• Recent and relevant labeling comprehension study experience:
  • Observational studies to test patient package inserts and product usability
  • Observational studies to test Medication Guide comprehension
  • REMS assessments

• Complete offering for optional GCP program: SOPs and policies covering ethics, privacy, security, part 11 compliance, and Good Clinical Practice (GCP) and data server safeguards
Labeling Comprehension and Observational Research Consulting Experience
Leadership in REMS Program Design and Implementation

• **Establishing industry best practices:**
  
  » Design of efficient and successful assessment protocols with expertise in:
    - Questionnaire development
    - Electronic data capture and secure hosting (since 2002)
    - Survey validation process including literacy review options and pretesting
    - Multimodal recruitment approaches
    - Statistical analysis and reporting metrics
  
  » Proven methods for cost-effectively recruiting prescribers and patients for Rx assessments and observational studies
  
  » Proprietary web survey portal providing easy but well controlled online survey access at [www.treatmentsurvey.com](http://www.treatmentsurvey.com)
  
  » Real-time assessment reporting dashboard “PharmaTrak Viewer”
  
  » CLINMETRIC™ database of aggregated REMS assessment results guides Clients with selection of appropriate performance metrics, interpretation of results, and determination of corrective actions
  
  » Expert research session moderators
  
  » Bilingual, HIPAA compliant call support
Leadership in REMS Program Design and Implementation

Centralized assessment portal for easy stakeholder and client access

Unique client specific dashboard for real-time assessment reporting

Proprietary web coding and database system verifies survey code authorization, and directs to appropriate survey
Multimodal Recruitment Capabilities

- Prescribers
- Pharmacy Claims Databases
- Pharmacy Intercept
- Opt-in Patient Databases
- Targeted Advertisement
- Consumer Health Panels
- Patient Advocacy Groups/Foundations
- Online Forums
### Observational Research and Labeling Comprehension Study Experience

<table>
<thead>
<tr>
<th>Disease Area</th>
<th>Sample</th>
<th>Product</th>
<th>Type of Research Study</th>
<th>Methodology</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Allergy</strong></td>
<td>Patients and Parent Caregivers</td>
<td>Injectable Drug/Device combination</td>
<td><strong>Observational study pre-market assessment</strong> of usability and attitudes towards a new drug delivery device</td>
<td>One-on-one interviews</td>
</tr>
<tr>
<td><strong>Asthma</strong></td>
<td>Patients and Parent Caregivers</td>
<td>Inhaled Drug/Device combination</td>
<td><strong>Observational study and pre-market assessment</strong> on probable use patterns and attitudes towards new inhaler technology</td>
<td>Web-based Survey</td>
</tr>
<tr>
<td><strong>Dermatology</strong></td>
<td>Patients</td>
<td>Injectable Aesthetic</td>
<td><strong>Observational study and pre-testing</strong> of a patient package insert for readability and comprehension</td>
<td>One-on-one interviews</td>
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<tr>
<td><strong>Diabetes</strong></td>
<td>Patients</td>
<td>Injectable Drug/Device combination</td>
<td><strong>Observational periapproval study</strong> on product usability and comprehension of patient package insert</td>
<td>One-on-one interviews</td>
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<tr>
<td><strong>Epilepsy</strong></td>
<td>Patients and Parent Caregivers</td>
<td>Rectally administered Drug/Device combo</td>
<td><strong>Observational periapproval study</strong> on product usability and comprehension of patient package insert</td>
<td>One-on-one interviews</td>
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<tr>
<td></td>
<td>Pharmacists</td>
<td>Rectally administered Drug/Device combo</td>
<td><strong>Observational periapproval study</strong> on dose preparation and understanding of instructional materials</td>
<td>One-on-one interviews</td>
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<td></td>
<td>Patients and Parent Caregivers</td>
<td>Rectally administered Drug/Device combo</td>
<td><strong>Phase IV Patient Registry</strong> to measure pharmacy dispensing performance and patient understanding</td>
<td>Survey</td>
</tr>
<tr>
<td><strong>Gastro-esophageal Reflux (GERD)</strong></td>
<td>Patients</td>
<td>Orally administered Drug capsule</td>
<td><strong>Pre-Market Product Evaluation</strong> for new oral GERD medication including swallow test</td>
<td>One-on-one interviews</td>
</tr>
<tr>
<td><strong>Pain</strong></td>
<td>Patients</td>
<td>Inhaled medication</td>
<td><strong>Observational periapproval study</strong> on product usability and comprehension of patient package insert</td>
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# Examples of REMS Assessment Experience

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<td><strong>Antiviral</strong></td>
<td>Patients</td>
<td>New Rx Medication</td>
<td>REMS Assessment for measuring understanding of the serious medication risks</td>
<td>Web-Based and Call Supported Survey</td>
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<td><strong>Cardiovascular</strong></td>
<td>Patients and Prescribers</td>
<td>New Rx Medication</td>
<td>REMS Assessment for measuring understanding of medication risks, appropriate use, and medication guide distribution compliance</td>
<td>Web-Based and Call Supported Survey</td>
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<td><strong>Cardiovascular</strong></td>
<td>Patients</td>
<td>Existing Rx Medication</td>
<td>REMS Assessment for measuring understanding of serious risks and medication guide distribution compliance</td>
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<tr>
<td><strong>CNS</strong></td>
<td>Patients and Physicians</td>
<td>New Rx Medication</td>
<td>REMS Assessment for measuring understanding of medication risks, appropriate use, and medication guide distribution compliance</td>
<td>Web-Based and Call Supported Survey</td>
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<td><strong>Gastroenterology</strong></td>
<td>Patients</td>
<td>New Rx Medication</td>
<td>REMS Assessment for measuring understanding of serious risks and medication guide distribution compliance</td>
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<td><strong>Metabolic</strong></td>
<td>Patients</td>
<td>New Rx Medication</td>
<td>REMS Assessment for measuring understanding of the serious medication risks</td>
<td>Web-Based and Call Supported Survey</td>
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<td><strong>Oncology</strong></td>
<td>Patients</td>
<td>New Rx Medication</td>
<td>REMS Assessment for measuring understanding of the serious medication risks</td>
<td>Web-Based and Call Supported Survey</td>
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<tr>
<td><strong>Surgical/Other</strong></td>
<td>Patients and Physicians</td>
<td>New Rx Medication</td>
<td>REMS Assessment for measuring understanding of medication risks, appropriate use, and medication guide distribution compliance</td>
<td>Web-Based and Call Supported Survey</td>
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<tr>
<td><strong>Transplantation</strong></td>
<td>Patients and Prescribers</td>
<td>New Rx Medication</td>
<td>REMS Assessment for measuring understanding of medication risks, appropriate use, and medication guide distribution compliance</td>
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<td><strong>Transplantation</strong></td>
<td>Patients and Prescribers</td>
<td>Existing Rx Medications</td>
<td>Elements to Assure Safe Use Program, Shared REMS. REMS assessment design and implementation for patients and health care providers to measure REMS performance</td>
<td>Web-Based and Call Supported Survey</td>
</tr>
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Key Learnings from Labeling Effectiveness Studies
Labeling Effectiveness Testing

• **Study Rationale & Benefits**
  
  – Improve product safety, efficacy, and usability
  
  – Mitigate risks from inappropriate drug or product use
  
  – Reduce regulatory jeopardy
  
  – Improve approval timeframe

- Increase Patient Satisfaction/Mitigate Risks
- Increase Product Utilization
- Increase Revenues $$$$$$$$
Studies of labeling comprehension, compliance and product usability have revealed surprisingly poor initial labeling performance by patients.

Figure 1 below is an example of a caregiver study involving manipulations with a novel drug delivery device. One device represented the currently marketed product; the other four devices tested were replacement prototypes. The study revealed labeling as a major source of end user confusion.

Figure 1. Caregivers Ability Properly Perform a Drug-Device Delivery without Error (n=48)
The process of labeling pretesting can yield critical insights into improving successful product use and reducing the potential for medication risk.

Figure 2 is a pharmacist study. The first pilot with the labeling (Study 1) demonstrated a 42% rate of dispensing error. Following label revisions and beta testing, a second study (Study 2) was performed with fifty retail pharmacists to measure effect of the labeling changes. The comparative results for study 1 and 2 are shown in Figure 2. The error rate from study 1 to study 2 declined from 42% to 8%.

**Figure 2. Labeling Comprehension Study with Pharmacists: Results Before and After Label Revisions**
Often more than one pilot study is needed to optimize comprehension of patient labeling.

Figure 3 provides the comparative results for three sequential studies on patients’ ability to properly set a dose, self-administer a medication, and recognize an empty delivery device. Labeling revisions occurred between study 1 and 2, and study 2 and 3. The success rates for each study are given in Figure 3. A dramatic improvement was observed from study 1 to study 3 with overall error reduced in half or more for each key measure, including a 95% success rate with dose administration in the last study.

Figure 3. Labeling Comprehension Study with Patients: Results Before and After Two Label Revisions

<table>
<thead>
<tr>
<th></th>
<th>Study 1 (n=40)</th>
<th>Study 2 (n=41)</th>
<th>Study 3 (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device Set-up</td>
<td>31%</td>
<td>33%</td>
<td>33%</td>
</tr>
<tr>
<td>Dose Administration</td>
<td>60%</td>
<td>67%</td>
<td>73%</td>
</tr>
<tr>
<td>Recognized as Empty</td>
<td>33%</td>
<td>56%</td>
<td>80%</td>
</tr>
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</table>
Compliance and Quality Assurance
BioTrak Research offers industry best practices in compliance:

- Good Clinical Practice (GCP) and Good Documentation Practice (GDP) compliance procedures and training program. Complete SOP system covering all facets of REMS assessments (30+ SOPs).
- Privacy and Security compliance procedures and training program and designated Officer
  - 100% of staff NIH certified in human subjects research and privacy
- Data management safeguards
  - Secure server - Physical and IP security measures (i.e., intrusion detection, encryption security, locked restricted access room)
  - Remote (offsite) backup and disaster recovery plan
  - Offer SSH that is user name/password authenticated
  - SSL on all data collecting websites
- Ethics policy, training, and designated Ethics Officer
- In compliance with all federal, state and local laws – no history of non-compliance
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