



**Innovations and Expertise in Risk Evaluation and
Mitigation Strategy (REMS) Program
Design and Implementation**



June 2010

About BioTrak

Leader and innovator in REMS program design and implementation

Consulting experience, industry best practices, novel technology tools, REMS educational videos, REMSadvisor.com

Industry best practice methodologies for REMS Assessments

PharmaTrak Research, PharmaTrak Viewer, Treatmentsurvey.com

Optimization methodologies for ETASU implementation system design

REMS Design Optimization (RDO) Program

State-of-the-art electronic data capture options through technology alliance

BioTrak-assisTek alliance

Novel technology tools for communication of REMS elements

*TouchPRO
MobilePRO
eQM*

About BioTrak



Two Core Consulting Areas:

- **PharmaTrak™ Research** drug safety risk management consulting services:
 - » REMS Consulting: Development and implementation of Risk Evaluation and Mitigation Strategy (REMS) programs, including those with Elements to Assure Safe Use (ETASU).
 - » REMS Assessments
 - » Risk analysis tools and predictive market models.
 - » Advanced analytics and statistical support.
 - » Registries: Development and implementation of custom registry solutions for patients, health care providers and pharmacists
- **BioTrak Custom Consulting** services:
 - » Observational research studies
 - » Labeling comprehension studies
 - » Product usability studies

BioTrak Fact Sheet



- 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 270 total research studies and over 45 web-based questionnaire survey studies with patients, health care providers, and pharmacists
- Recent and relevant REMS and pharmaceutical risk management consulting experience
- Considered a leader and innovator in REMS assessments
- Key partnerships with ParagonRx (REMS assessments) and assisTek (ETASU novel technology solutions)
- Complete offering for optional GCP program: SOPs and policies covering ethics, privacy, security, part 11 compliance, and Good Clinical Practice (GCP) and well as data server safeguards



REMS Consulting Experience





- **Establishing industry best practices in REMS Assessments:**
 - » Design of efficient and successful REMS assessment protocols
 - Expertise in questionnaire development
 - Expertise in web-based survey design and secure hosting (since 2002)
 - Expertise in statistical analysis and sample size recommendations
 - Robust survey validation process including literacy review options and pretesting
 - » Proven methods for cost-effectively recruiting prescribers and patients for Rx assessments and observational studies. Includes access to large physician and patient ailment panels as needed.
 - » Proprietary web survey portal providing easy but well controlled online survey access at www.treatmentsurvey.com
 - » Real-time assessment reporting dashboard “PharmaTrak Viewer”
 - » Bilingual, HIPAA compliant call support
 - » Producer of a three-part videos series on REMS assessments at: <http://www.youtube.com/biotrakvideo>

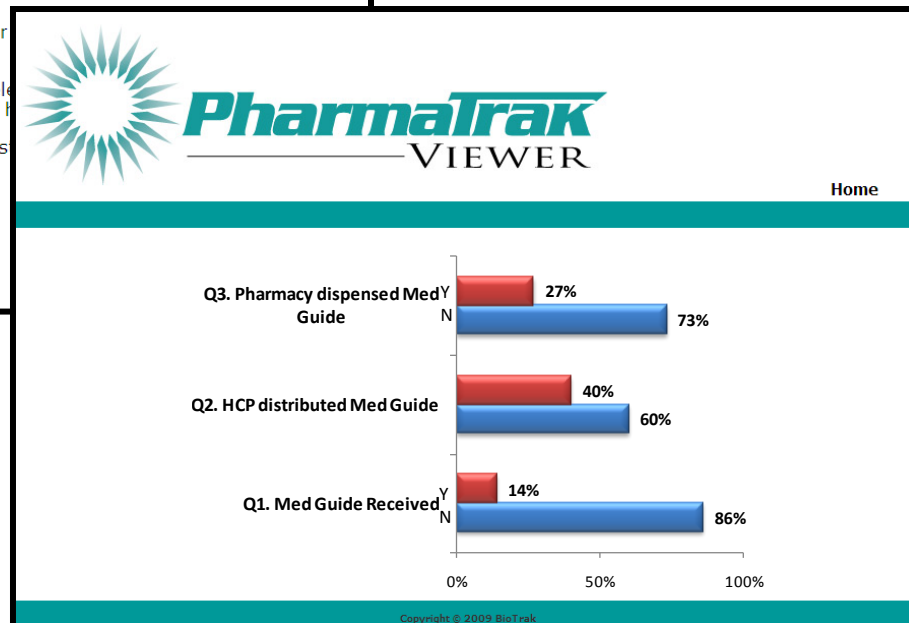
Leadership in REMS Program Design and Implementation



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



Leadership in REMS Program Design and Implementation



- **Innovative solutions for ETASU program and implementation system design:**
 - » REMS Design Optimization Process (RDO); a unique, high value modeling technique providing critical insights into the expected commercial impact of a ETASU design:
Model outputs predict likely:
 - ▶ Potential to mitigate risk
 - ▶ Stakeholder acceptance
 - ▶ Intent to prescribe product and expected patient utilization metrics
 - ▶ Market share impact
 - » Novel technologies tools for ETASU implementation system data capture and communication of REMS elements:
 - ▶ TouchPRO, MobilePRO, eQM, other
- **Commitment to REMS education and consulting:**
 - » January 25, 2010 - Launched “REMSadvisor.com”, the first dedicated REMS information website - www.remsadvisor.com
(official go live date planned for February 2, 2010)

REMS Consulting Experience

Disease Area	Sample	Product	Type of Research Study	Methodology
Antiviral	Patients	New Rx Medication	REMS Assessment for measuring understanding of the serious medication risks	Web-Based and Call Supported Survey
Cardiovascular	Patients and Prescribers	New Rx Medication	REMS Assessment for measuring understanding of medication risks, appropriate use, and medication guide distribution compliance	Web-Based and Call Supported Survey
Cardiovascular	Prescribers	New Indication of Existing Rx Medication	REMS Assessment for measuring understanding of medication risks, appropriate use, and medication guide distribution compliance	Web-Based and Call Supported Survey
CNS	Patients and Physicians	New Rx Medication	REMS Assessment for measuring understanding of medication risks, appropriate use, and medication guide distribution compliance	Web-Based and Call Supported Survey
CNS	Patients	New Rx Medication	REMS Assessment for measuring understanding of serious risks and medication guide distribution compliance	Web-Based and Call Supported Survey
Epilepsy	Patients	New Rx Medication	REMS Assessment for measuring understanding of serious risks and medication guide distribution compliance	Web-Based and Call Supported Survey
Epilepsy	Patients	Existing Rx Medication	REMS Assessment for measuring understanding of serious risks and medication guide distribution compliance	Web-Based and Call Supported Survey
Epilepsy	Patients	Existing Rx Medication	REMS Assessment for measuring understanding of serious risks and medication guide distribution compliance	Web-Based and Call Supported Survey
Gastroenterology	Patients	New Rx Medication	REMS Assessment for measuring understanding of serious risks and medication guide distribution compliance	Web-Based and Call Supported Survey
Gastroenterology	Patients	New Rx Medication	REMS Assessment for measuring understanding of serious risks and medication guide distribution compliance	Web-Based and Call Supported Survey
Metabolic	Patients	New Rx Medication	REMS Assessment for measuring understanding of the serious medication risks	Web-Based and Call Supported Survey
Pain	Patients	Existing Rx Medication	REMS Assessment for measuring understanding of serious risks and medication guide distribution compliance	Web-Based and Call Supported Survey
Surgical/Other	Patients and Physicians	New Rx Medication	REMS Assessment for measuring understanding of medication risks, appropriate use, and medication guide distribution compliance	Web-Based and Call Supported Survey
Transplantation	Patients and Prescribers	New Rx Medication	REMS Assessment for measuring understanding of medication risks, appropriate use, and medication guide distribution compliance	Web-Based and Call Supported Survey
Transplantation	Patients and Prescribers	Existing Rx Medications	Elements to Assure Safe Use Program, Shared REMS. REMS assessment design and implementation for patients and health care providers to measure REMS performance	Web-Based and Call Supported Survey

Other Pharmaceutical Observational Research and Labeling Comprehension Study Experience



Observational Research and Labeling Comprehension Study Experience

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





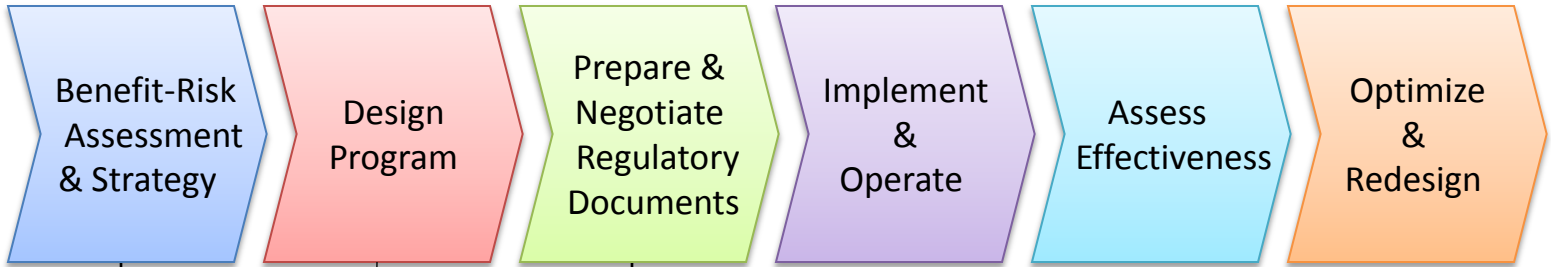
Elements to Assure Safe Use Program Design and Implementation Capabilities



BioTrak REMS Management Process - 1



Phase III/Pre-NDA Periapproval Launch Post-market



- Characterize toxicities and safety concerns
- Identify risks associated with care delivery
- Itemize risks; determine which may require intervention beyond labeling (i.e., REMS)
- Define strategic options for risk mitigation
- Labeling, Appropriate Use Program, REMS
- Select risk mitigation strategy, e.g., REMS and/or non-REMS
- As appropriate; create development-stage risk management plan

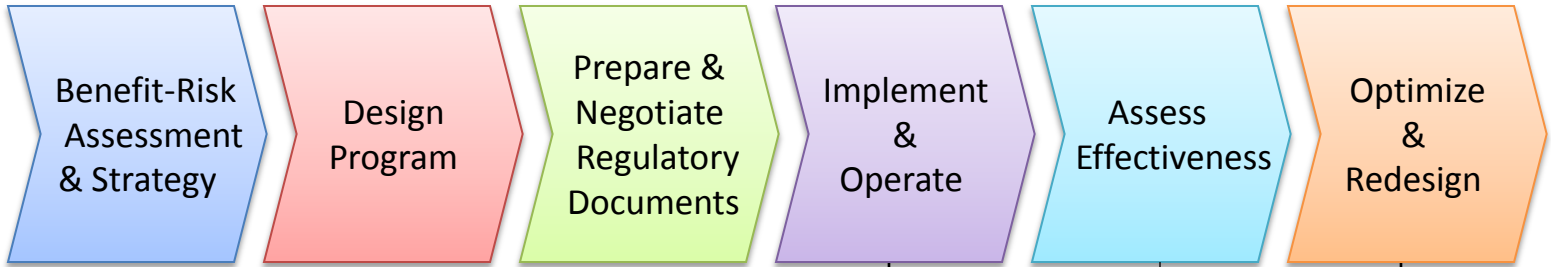
- Develop plan with BOTH clinical and market inputs
 - REMS Design Optimization (RDO)
 - Pre-assessments
- Create REMS elements
 - Effective risk communications
 - Novel communication tools
 - Elements to Assure Safe Use
 - Implementation systems
 - Assessment protocols

- Create REMS document and supporting materials
- Develop assessment protocol
- Plan contingencies
- Document implementation details to support negotiations
- Rapid response process to edit REMS
- Begin implementation readiness planning

BioTrak REMS Management Process - 2



Phase III/Pre-NDA Periapproval Launch Post-market



- ETASU implementation
 - Specifications
 - Operational interface considerations
 - Reporting capabilities
 - System development
 - Integrate communication and training elements, agreements
 - Validation and usability testing
 - Beta testing
 - Other tool integration (IVRS, wireless)
- HCP Communication Plans and Medication Guide Programs

- Implement assessment protocol(s)
 - For REMS elements
 - For ETASU
 - For REMS performance
- Define and produce reports of REMS effectiveness
 - For REMS elements
 - For ETASU
 - For REMS performance
- Define measures, metrics, and reporting for internal REMS Effectiveness Management process

- Root cause analysis
- Re-design program
- Re-design REMS promotion
- Re-define internal communications & commitments
- Rapid response to changes in REMS elements content, design, and promotion

BioTrak's REMS Design Optimization (RDO) Process for ETASU



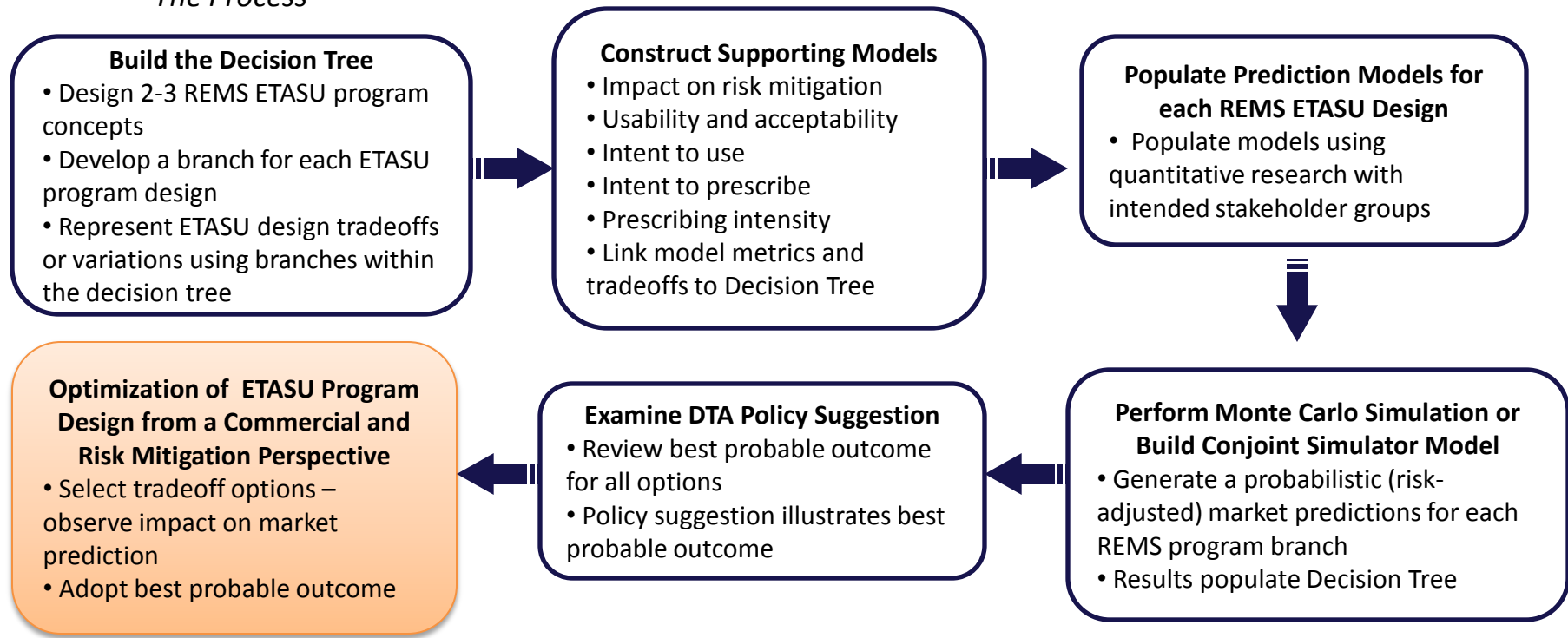
Key Business Question:
Which REMS ETASU program design do we adopt? How will it effectively mitigate risk? What impact will it have on the potential market?

Answer

REMS Design Optimization:
Identify the REMS ETASU program design and options with best predicted probable market outcome

*Decision Tree Analysis (DTA)
Market Simulation Models
Primary research with Stakeholders
Market outcome predictions*

The Process





In March 2009, BioTrak formed a technology partnership with assiTek to offer state-of-the-art solutions for REMS ETASU programs.

REMS Program Design, Implementation & Assessment Expertise BioTrak

- REMS-related consulting experience: ETASU design, Med Guides, HCP Communication plans
- REMS assessment best practices
- Commercial planning expertise
- Market research expertise
- Analytics/STATS
- Performance reporting

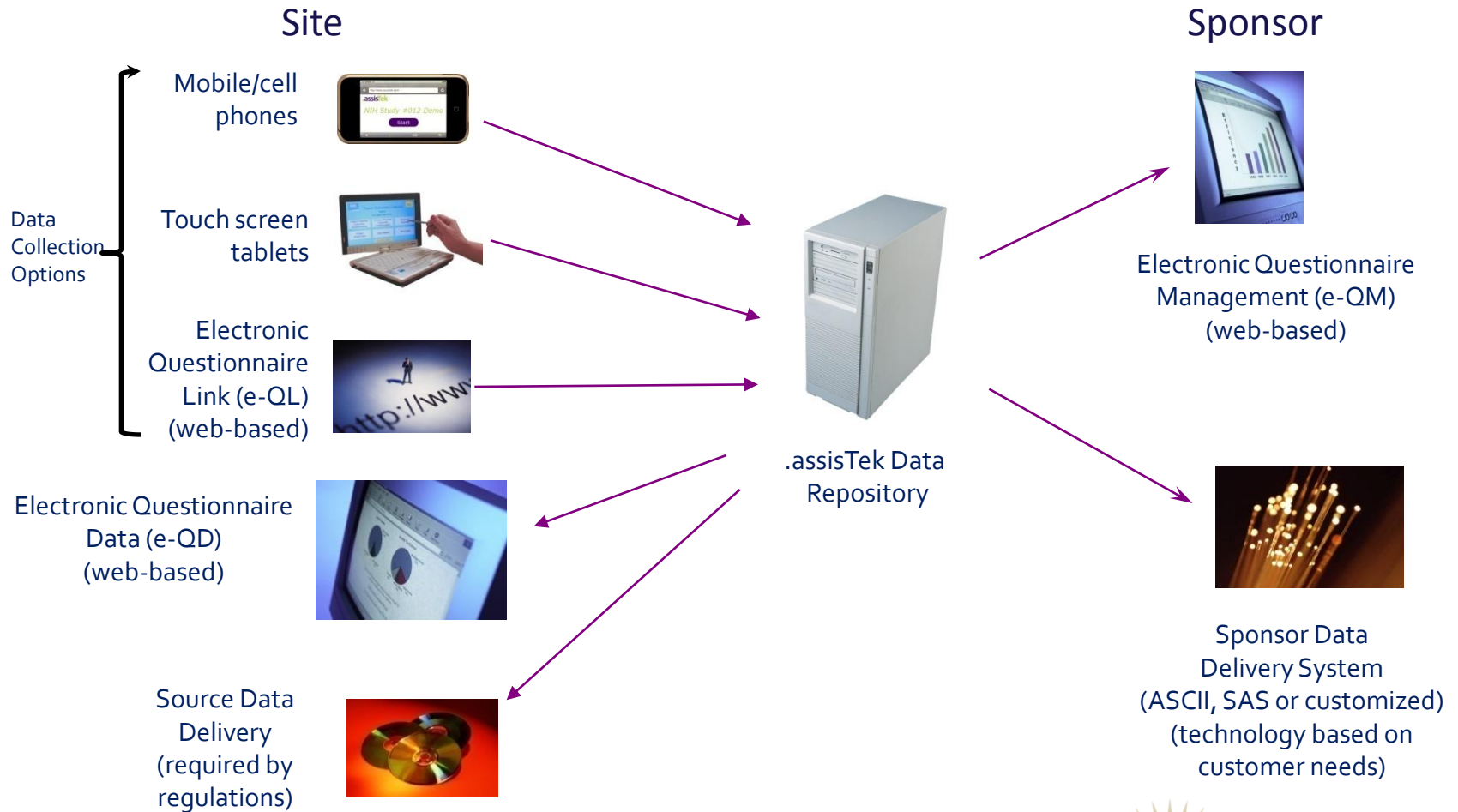
**Integrated REMS
ETASU Solutions**

Innovation Toolbox assiTek

- Over 100 Electronic data capture programs
- Databases and novel registration technology solutions
- Wireless and internet based health questionnaires and data collection
- Multimedia communication tools and devices, touch screens

BioTrak-assisTek Alliance Electronic Data Capture Solutions

- **assisTek has extensive experience with web, touch screen tablet, and recently mobile phone design and deployment for electronic questionnaire and data capture.**



BioTrak assisTek Alliance Novel Technology Solutions



TOUCHPRO

Implemented to collect data from patients, physicians, nurses, in 26 countries for 15 years. Most broad and in depth experience using this technology in pharmaceutical studies.

- Multimedia device with internet capability
- Almost 100 assisTek studies with this device, high customer satisfaction
- Effectively engages patients and prescribers – Novel approach to communicate REMS elements
- One touch wireless access to registry portal
- Windows XP software
- Customized web browser screens will make registry interface easy to follow and read
- Proven robust platform
- Can run locally to reduce costs

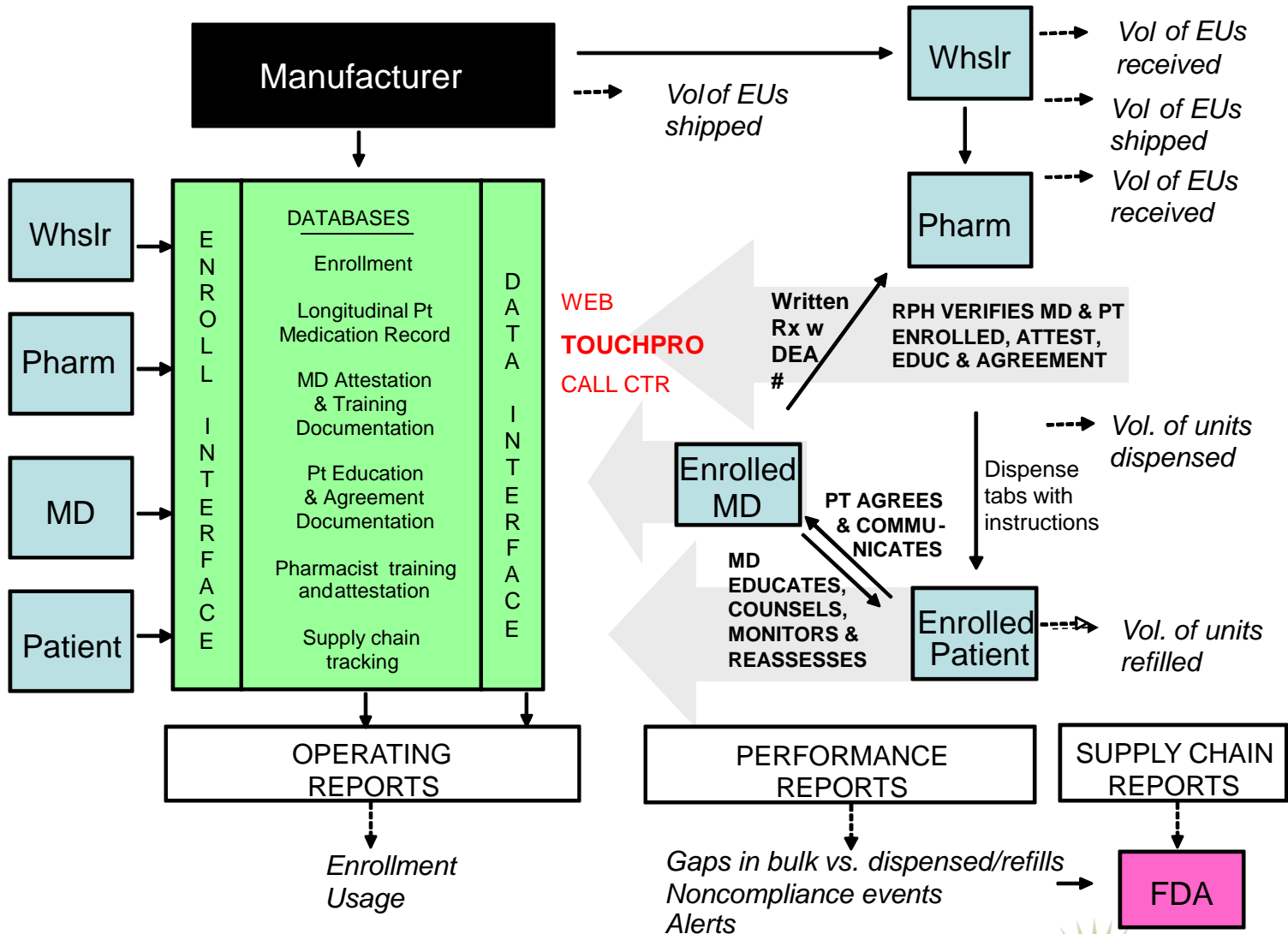


MOBILEPRO

Selected for multiple PRO and clinical studies to remotely capture patient survey data. Load video and MP3 files for audio-visual communication of key risk messages and training modules. Fast, convenient registration, verification, and questionnaire administration for patients at point-of-service or point-of-prescription.

- Multimedia device with internet capability
- Effectively engages patients and prescribers
- One touch wireless access to registry portal
- Novel approach to communicate REMS elements
- Windows XP software
- Customized web browser screens

Example of ETASU Implmentation System Capability Through BioTrak-assiTek





Compliance and Quality Assurance



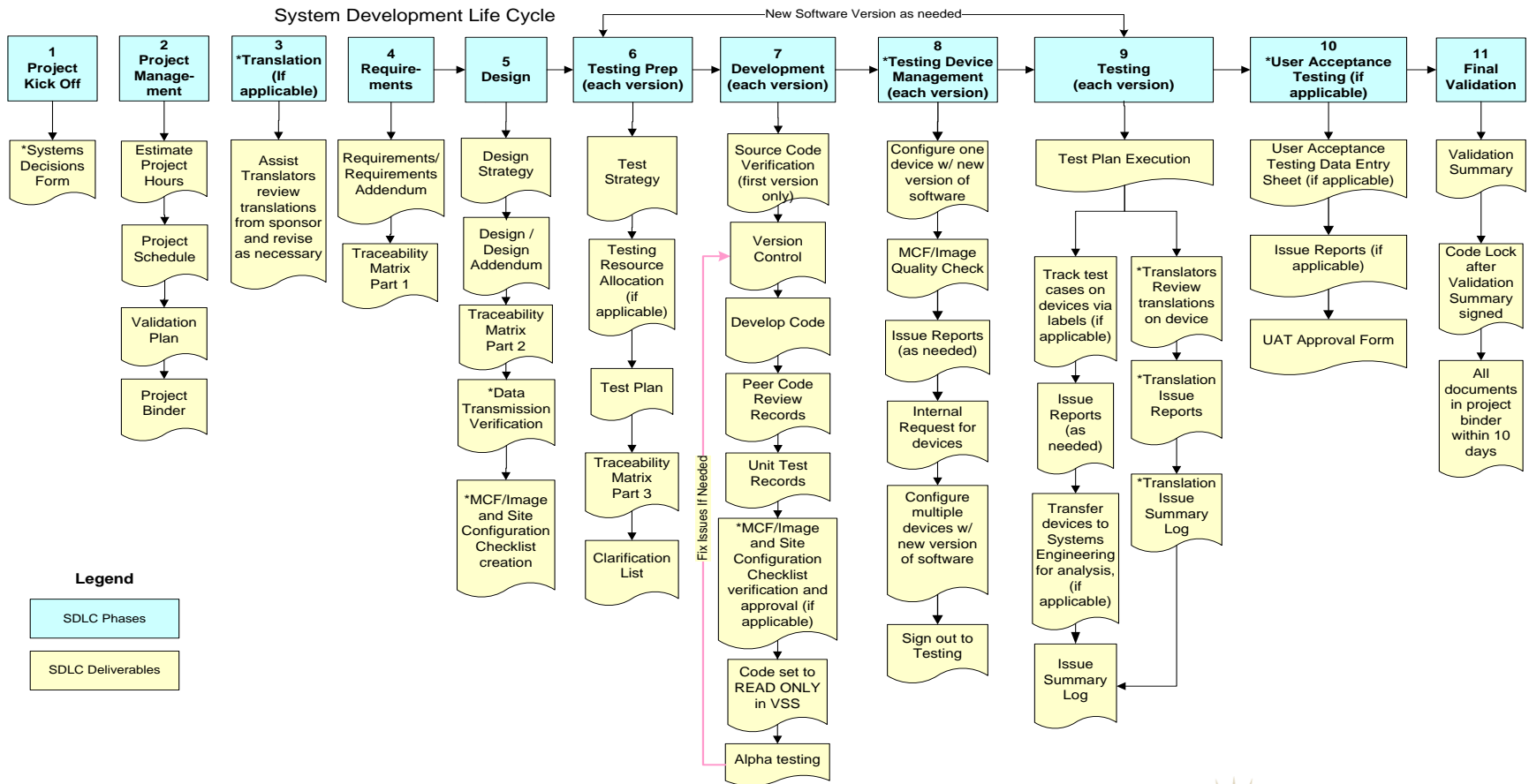
Compliance Statement



- ✓ Ethics policy, training, and designated Ethics Officer
- ✓ Good Clinical Practice (GCP) and Part 11 compliance procedures and training program
- ✓ 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
- ✓ In compliance with all federal, state and local laws – no history of non-compliance

BioTrak-assisTek Alliance REMS ETASU System Validation and Quality Assurance

The BioTrak-assisTek ETASU alliance has strong processes for implementation system validation (audited many times with compliments from Top 10 pharma).



Contact



- **Larry Risen**
President
BioTrak Market Intelligence, Inc.
5927 Balfour Court - Suite 201
Carlsbad, CA 92008
t 760.448.4823
f 760.603.9535
Email: *risen@biotrak.com*