



### Core Capabilities:

- An advanced, visual data exploration and analysis tool designed for safety specialists and regulatory safety reviewers
- Promotes systematic safety review and facilitates signal detection by screening for high-risk safety issues in clinical trials data
- Analyze individual or pooled study data
- Uncover safety issues specific to different age groups, genders and races
- Browse aggregate values, trends and outliers in blinded study data
- Evaluate safety effects across drug dose groups in unblinded study data
- Drill down from graphical to tabular data listings, individual subject data and patient profiles
- Document, manage and track signals as clinical data accumulates
- Compare a new product's safety profile to comparators on the market as displayed by Empirica Signal
- Web-based architecture built on the powerful WebSDM™ data repository platform

## Empirica™ Study

### Clinical Trials Signal Detection

## Exploring Clinical Trials Data for Safety Signals

### Improving the Understanding of Product Safety during Clinical Development

The cost of developing new therapeutic products is increasing all the time, but the costs of developing a product that is not approved are much worse. Worst of all are the costs of removing a product from the market soon after approval because of a safety defect that was not identified soon enough. Today's regulatory reviewers are extremely sensitive to the need to improve their understanding of a product's risk/benefit ratio, and they are using sophisticated new tools to delve deeper into clinical data thanks to the advantages of standardized data formats such as the Clinical Data Interchange Standards Consortium (CDISC) Study Data Tabulation Model (SDTM), which enables the use of standard statistical screening methods. The Food and Drug Administration (through published guidance documents) and the Council for International Organizations of Medical Sciences (CIOMS) VI have given insight into some of the fundamental areas of safety review that must be examined for any new drug application. In today's world, sponsors also need to capitalize on the most sophisticated tools available to better understand the emerging safety profile of their products during development. This allows timely analysis of safety issues to be explored early in the development process, and, if insurmountable concerns arise, a development program can be cancelled early so that resources can be redeployed on a more promising candidate.

Phase Forward's Empirica suite of innovative pharmacovigilance and risk management solutions delivers Adverse Event Reporting, Data Mining, Signal Detection and Signal Management capabilities that help companies identify potential safety problems and manage risk effectively across the full product life cycle. The Empirica Suite was designed to help companies strategically manage their pharmacovigilance activities.

### Empirica Study: Unleashing the Potential of Standardized Clinical Data

Empirica Study, the latest release of the award-winning CTSD Clinical Trials Signal Detection product originally developed by Phase Forward's Lincoln Safety Group, is an established tool that provides a dynamic, visual data review environment for reviewing safety data and detecting signals in clinical trials data in CDISC SDTM format. The standard SDTM data structures enable the reuse of advanced statistical analysis algorithms and simplify pooling of data, bringing a new degree of visibility into clinical data for safety reviewers. Empirica Study helps sponsor safety reviewers explore and improve their understanding of the most critical safety concerns that preoccupy regulatory reviewers when examining product licensing applications.

## Benefits of Empirica Study

- Provides a scientific framework for proactive review of the safety profile of emerging products
- Supports a more active and transparent safety review process
- Provides easily navigable access to clinical trials safety data
- Supports analysis of single study or pooled studies
- Interactive visual displays allow exploration of Demographics, Adverse events, Concomitant Medications, Labs, ECG, Vital Signs, Completion and other study data
- Enables rapid, on-line assessment of safety data for routine review, exploratory analysis, and characterization of potential signals:
  - Rapid on-line access to advanced graphical/visualisation tools
  - The ability to rapidly navigate from aggregate data displays to individual patient profiles
  - Ability to review data by Age, Gender or Race
  - Provides a broad library of standard analysis types and tabular displays

## Built on the WebSDM™ platform

Used by FDA to validate and review study submissions in the FDA-preferred CDISC SDTM format.

### System Requirements:

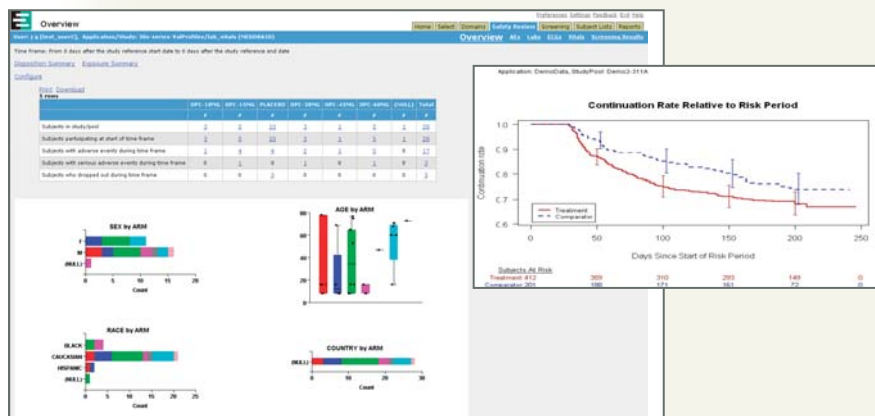
Web application with Oracle® database

Server-centric architecture

- Supported on Microsoft® Windows® 2003 Advanced Server platform
- Suitable for integration with other applications, such as clinical safety systems

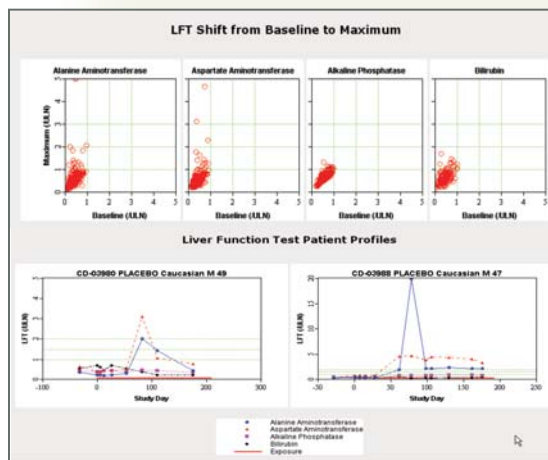
## Review Safety Data from Completed Studies

The Empirica Study Safety Review interface is designed to support the workflow outlined in the FDA 2005 Safety Review Guidance\*. A first step in reviewing any study is to get a demographic overview of the study population by treatment group and a summary of some critical enrollment parameters. From this interface you can also get a Kaplan Meier plot or exposure summary graph to gain a high-level overview of the study data.



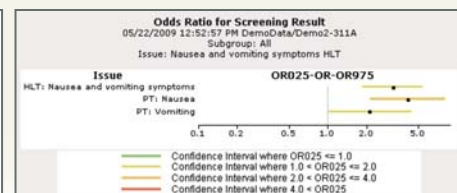
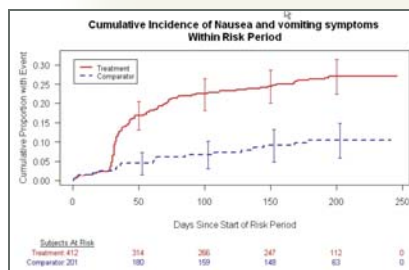
## Explore Safety Data for In-stream Blinded Trials

Empirica Study provides a rich portfolio of graphical displays to understand overall safety trends and outliers when the study is active and treatment is blinded. For example, one can see several outliers in the liver function test shift display below, and then drill down to examine the individual patterns for each of the individual patients.



## Explore Adverse Event Data

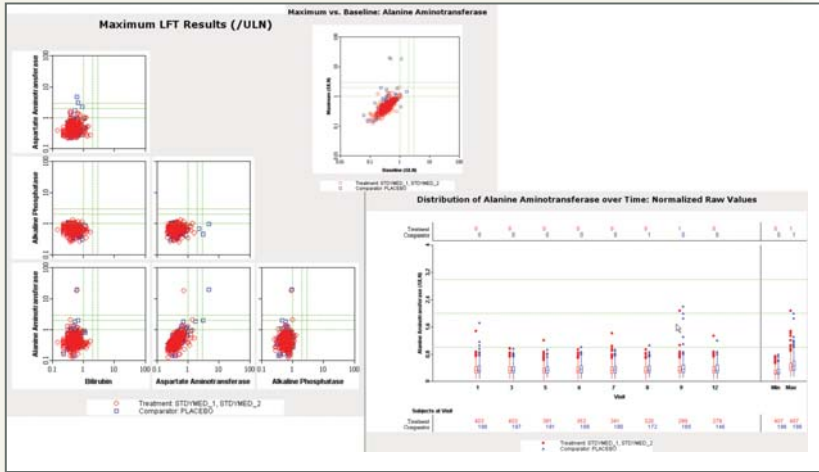
Reported Adverse Events (AEs) and Serious Adverse Events (SAEs) can be compared across treatment groups and explored at all MedDRA levels (including Standardized MedDRA Queries and custom event lists) using Empirica Study's signal scores, tabular displays and graphical tools. The example below shows a cumulative incidence display for nausea and vomiting, together with a display of the odds ratio screening result with confidence intervals.



\* U.S. Department of Health and Human Services  
Food and Drug Administration  
Center for Drug Evaluation and Research (CDER),  
Reviewer Guidance, Good Review Practices, February 2005

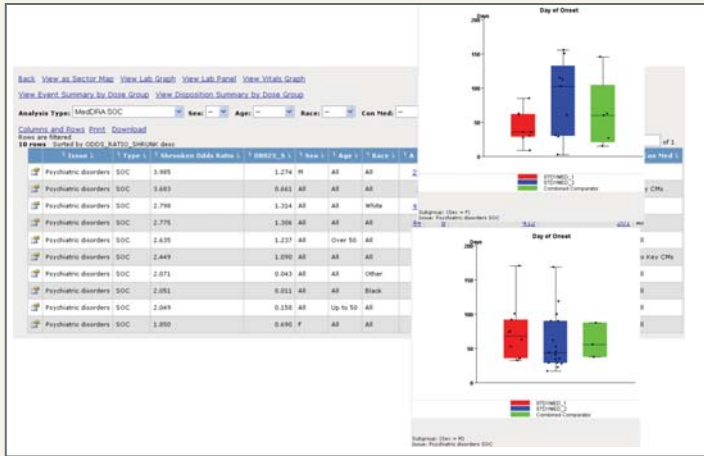
## Explore Lab Data

A variety of lab data reports are available, including clinical significance, change from baseline and specialized displays for hematotoxicity and liver functioning (including Hy's law).



## Review Screening Results for Signals Affecting Sub-populations

Signal screening scores are computed by Empirica Study for the full study population or subgroups by age group, gender, race, allowing safety reviewers to see if stronger signals are associated with particular sub-populations. The lab display below shows test results differentiated by each subgroup.



## Identify Safety Signals

Empirica Study uses simple statistical methods to identify disproportionalities between treatment groups to highlight safety signals. Tracking tools integrated into the system assure that signals can be monitored through to resolution, providing a basis for a more comprehensive statistical, medical and management review. The Sector Map graph below provides a big picture safety overview. Terms are grouped according to the MedDRA hierarchy to support pattern recognition. AEs that appear more frequently in treatment than comparator are shaded red according to signal strength; those that appear more often in comparator or placebo are green.



## Empirica Study Features:

- Drill down from visual, aggregate data displays to subject lists and individual, time-aligned patient profiles
- **New** – Improved navigation between patient profiles for sets of patients
- **New** – Support for non-parallel study designs
- Library of denominator-based screening tests to highly disproportional incidence of events among subjects and population subgroups across treatment groups:
  - Adverse events at MedDRA™ Preferred Term, High Level Term, High Level Group Term, and System Organ Class levels
  - Significant difference from lab or vitals baseline
  - Standardized MedDRA Queries (SMQs) and custom event lists
  - Clinically significant lab test results
  - Hy's law test for hepatotoxicity
  - Clinically significant QT prolongation
  - Premature study discontinuation
  - Advanced Bayesian logistic regression techniques
- **New** – Expanded, improved lab graphs to explore emergence of safety signals including change from baseline, lab shifts, normal range outliers, scatter plots, and many others.
- **New** – Graphical displays for odds ratios
- **New** – Improved, streamlined process for handling in-stream data loading
- Usability features include MedDRA browser, data browser, report builder, subset list query wizard
- Documentation and tracking of signals with audit trail

## The Empirica Suite

Phase Forward's complete solution for pharmacovigilance and risk management includes, in addition to Empirica Study, the Empirica Trace adverse event management system with Empirica Gateway, and the Empirica Signal product with Signal Management to identify, manage and track the evolution of safety signals in public and proprietary spontaneous report databases.

## The Phase Forward Advantage

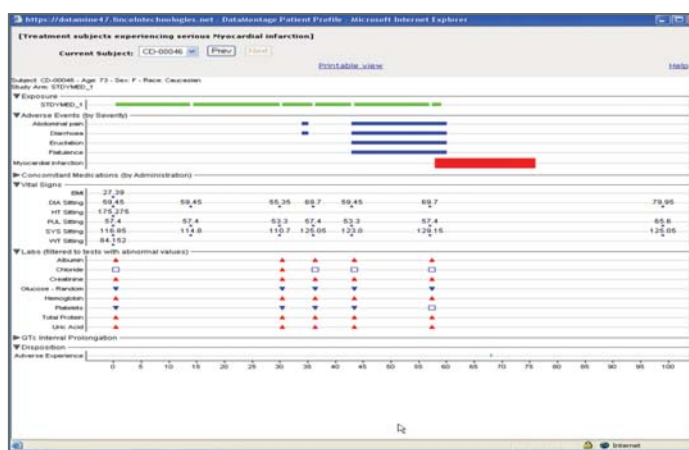
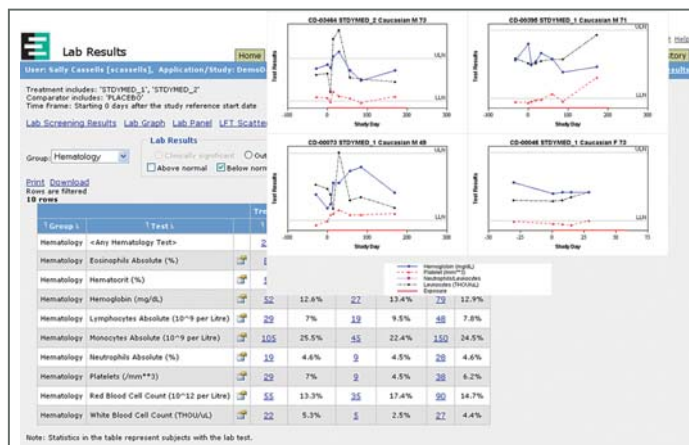
The development of the Empirica suite and delivery of Empirica-related services are managed by Phase Forward's Lincoln Safety Group, one of the most experienced and respected teams in the industry. Only Phase Forward can offer such a highly skilled and experienced team with a proven track record of working with safety experts in both the government and commercial sectors.

## Comprehensive Services and Support (Available Separately):

- Web-based and on-site training available with custom configuration to meet your safety review team's needs
- Implementation consulting for process development and integration with in-house clinical trials data feeds and for data provisioning strategies on active trials
- Expert advisory statistical consulting to explain the underlying statistical screening techniques used to identify safety signals
- Expert consulting on the conversion of clinical trials data into CDISC SDTM format
- Validation support services
- Installation services or application hosting available
- 24x7 Help desk support

## Visualizations and Drill Down — The Key to Data Exploration

Empirica Study was designed to unleash the power of standardized clinical trials data for non-technical safety experts by providing a rich, intuitive set of advanced graphical visualizations that describe the clinical study populations and drug safety profile from many angles. When a user clicks on any of these aggregate graphical displays, they are presented with a menu of options for further graphical and tabular displays of data, including lists of all the subjects included.



From a list of subjects, a user can display a tabular patient profile showing all of the critical safety data for each subject, and, from there, they may display graphical patient profiles that depict this data for a patient over time. In addition to these overall patient profiles, Empirica Study includes specialized patient profiles to display measures such as hepatotoxicity and vital signs for each patient, along with easy navigation tools to browse through a set of patient profiles for a group of subjects at a time.

## Contact Us for More Information

For more information about Empirica Study, the Empirica suite of safety products, and other Phase Forward products and services, please contact us at: info@phaseforward.com.

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