

## What compels a company to change Safety Database Systems?

Presented by WCI's Jeffrey Ho, Marcelo Diaz and Greg Shankland

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At the core of all Pharmacovigilance organizations (PVOs) is the Safety Database (SDB) system used to capture, assess and report adverse events (AEs) to regulatory authorities worldwide. Effective execution of AE processing, reporting to authorities and the broader analysis essential to signal detection and risk management are heavily dependent on system functionality. An evolving global regulatory environment is creating new challenges and business requirements increasing the importance of system flexibility and vendor responsiveness.

SDB infrastructure consumes a significant share of the total investment in drug safety activities and replacement has far reaching organizational impact. An implementation on a medium/large scale will likely:

- Cost \$10-15+ million in capital expenditure
- Require 35-40 full time equivalent staff for 18-24 months
- Consume business and IT resources needed for day to day operations
- Require extensive effort to engage stakeholders both internal and external to the PVO (e.g. Clinical, Regulatory), as well as external to the business itself (e.g. license partners, affiliates)

What then, are the factors that compel a PVO to make a decision of such significance?

In January 2006 WCI conducted a survey of Pharmaceutical and Biotechnology organizations to gain better insight into the influencing factors.

### Survey Participants

Senior managers in Pharmacovigilance functions (Heads of PV, PV IT leads and PV business leads) are key roles that deal with the central issue of the effectiveness of SDBs in enabling the PVO to perform its responsibilities.

A readily accessible source of these PVO functions was available through WCI's established pharmacovigilance best practice forums, pvnet™ and pvconnect. These paid membership forums attract leading industry names seeking strategic insight and operational benchmark data.

Participating organizations are representative of the industry in terms of organization size and type, as well as the SDBs currently installed. Annual volumes of AEs processed range from 10,000 to over 50,000 and annual revenues range from \$100 million to over \$10 billion (2004 data).

The three major SDBs are found in similar numbers (Argus, ARISg, and Clintrace - installed versions vary) with a lower incidence of Oracle AERS and custom solutions which is a similar mix to that gleaned from a larger sample elsewhere.

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These sample characteristics lend credibility to extrapolating results as representative of the wider community of PVOs.

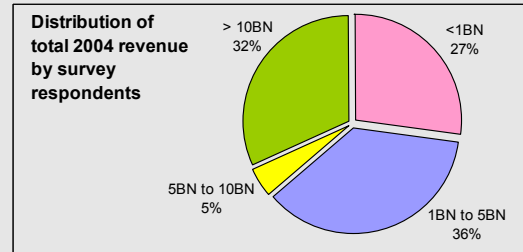
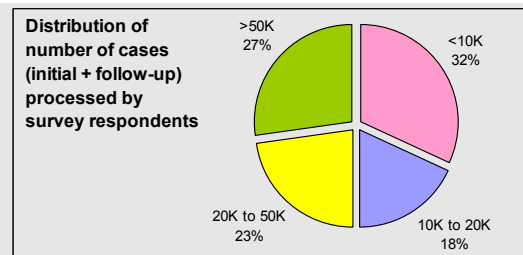
### The Survey

The survey collected information in three components:

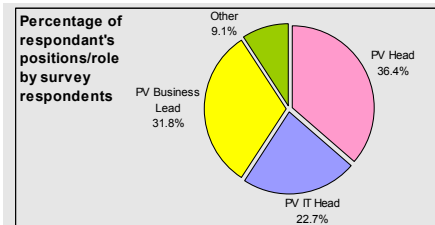
- Establishing the landscape
- A structured questionnaire facilitating ranking of influencing factors
- A free-form component allowing participants to qualify responses

### The Landscape

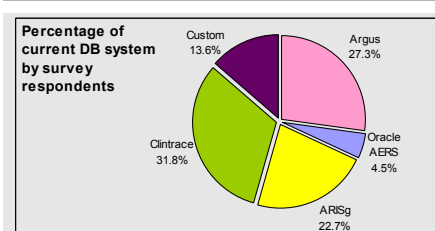
#### Which companies responded?



#### Who completed the survey?



#### Which SDB are they using?



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### **SDB life expectancy**

Cross industry data from comparable scenarios provide guidance to estimate life expectancy of similar systems and indicate a range of five to seven years.

The progressive deterioration in the capability of an installed application to support evolving needs will typically elicit responses to compensate in a progressive fashion.

Lead times between Vendor releases incorporating new functionality are relatively long and additional means to deliver the required result are commonplace.

Amongst survey participants 14 provided relevant historical data as follows:

- 8 report actively lobbying the vendor to enhance SDB functionality
- 9 have implemented manual 'workarounds'
- 7 embarked on customization of their SDB
- 6 engaged third party help to provide necessary support.

Eventually the cumulative performance gap and cost of additional work become risky or unreliable, or the investment required to upgrade or replace becomes financially viable.

Within the last four years the 22 participants have many incidences of replacements and significant upgrades (one requiring data mapping for migration), providing real context to their responses:

- 20 (91%) report a replacement or significant upgrade
- 17 (77%) have replaced systems, 7 (32%) doing so more than once
- 13 (59%) report significant upgrades

The anticipated life expectancy calculated as the time from last switch to the forecast replacement date produces an average of 5.6 years and a median of 6 years. This is consistent with estimates from cross industry guidelines.

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### Custom or COTS?

These decision points are opportunities to consider the benefits of different types of package. Amongst the 22 respondents, the number of custom applications currently installed is 3 (14%), down from 12 (55%) approximately five years ago – a significant shift in favor of commercial off-the-shelf (COTS) applications.

Contributing factors were not assessed here; however, they are generally well accepted as similar to other industries focusing on core business and eliminating software development and maintenance effort.

An important consequence of selecting COTS solutions is that the benefit of eliminating non-core activities is easily eroded by any need for customization which adds cost and complexity. SDB selection is critical to matching business needs and system functionality and is best facilitated by the compilation of user requirements as the basis of comparison and to minimize the needs not met by the SDB that may require customization. The one off investment to compile requirements provides significant return by establishing agreement with the vendor of expected functionality and through the avoidance of recurring support costs over a long period.

The approach has an often ignored yet significant benefit from minimizing the inherent points of tension created by conflicting objectives to simultaneously minimize user compromises and avoid customization and support costs.

Vendor applications that offer advanced configurability and flexibility will have a significant advantage in satisfying the evolving needs of PVOs

### Factors influencing replacement decisions

The structured list of influencing factors ranked by participants segments into five major categories:

- Functionality
- Regulatory Imperatives
- Technology
- Configurability to Extended Organisation
- Efficiency of Operation.

The top 5 rankings at aggregate level are presented, followed by selected points within category rankings. Supplementary comments from topic experts provide explanatory context.

### Aggregate ranking

Participants were asked to rank each factor on a 1 (weak influence) to 5 (very strong influence) scale. Aggregate rankings here are defined as the sum of strong (score 4 or 5) responses. Any equal scores are resolved by the ratio of 4 and 5 scores. All participants (22) provided responses.

## What compels a company to change Safety Database Systems?

### **Reason 1: Inadequate support of new regulations**

Ranked as strong influence by 16 participants (73%)

Comment: The regulatory environment is increasingly demanding and is a global phenomenon. Regulations impact PVOs at multiple levels and many have fundamental implications for database structure, configurability, reporting capability and integration with other systems and data sources.

### **Reason 2: Limited or no support of automated workflow**

Ranked as strong influence by 16 participants (73%)

Comment: Workflow tools enable automated routing and tracking of cases through multiple process steps, identification and location of cases, isolation of processing bottlenecks and delays and metrics to support timely and efficient management and processing of AEs and reports.

### **Reason 3: Electronic Submissions Support (Expedited)**

Ranked as strong influence by 14 participants (64%)

Comment: Authorities are phasing in requirements for electronic submission of reports. The FDA is expanding its electronic gateway which is already used by 24 organizations. The EMEA requires electronic expedited reports for all products marketed in member countries and provides supporting tools.

The sixth ranking reason is electronic submissions for aggregate reporting which is similarly mandated in phases. This separation into two factors reflects the regulatory phasing, however, considered in combination they would be the top ranking reason.

### **Reason 4: Reporting performance**

Ranked as strong influence by 15 participants (68%)

Comment: The SDBs generally originated as transactional tools supporting the capture, processing and simple reporting to authorities. Reporting requirements have become increasingly demanding to meet multiple business needs ranging from management metrics to automated prompts triggering specific actions. This requires a strong reporting structure which is not inherent to a design for transactional purposes. Some vendors have enhanced this capability by bolting on a separate reporting module offered as a bundled package.

### **Reason 5: Limited or no support for signal detection**

Ranked as strong influence by 15 participants (68%)

Comment: The high ranking of this reason indicates that PVO's expect that SDB vendors should incorporate signal detection capability in future releases.

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This expectation is fraught with pitfalls for both PVO's and SDB vendors and should give cause to exercise caution.

The significance of signal detection is emphasized by its selection as a top priority for study by members of WCI's pvnet forum in 2005. The study highlighted substantial differences in philosophy and approach amongst members, many of whom are survey respondents.

It is an immature discipline and accepted 'best practices' will take considerable time to evolve. Nevertheless, there are basic requirements for effective signal detection that lead one to challenge the expectation that the SDB's will be primary enablers implied by this ranking.

Effective signal detection will at a minimum require:

- Consistently coded data for owned products – from the SDB
- Integration with multiple systems across the organization. Critical information is held by other functions, e.g. sales volumes and some components of product definitions frequently use different product structures which will require conversion tools or a cross-functional dictionary to enable aggregation of data from multiple systems
- Baseline data for comparator products – sources external to the company are likely to be required
- The ability to aggregate data in multiple permutations
- The application of pre-defined or custom statistical algorithms
- Deep analysis and 'what if?' capability

The analysis capability is complex and once again the transactional origin of SDBs already described will be limiting. Extensive integration with other corporate systems and the need to import and possibly convert information from internal and external sources are not common features of today's SDBs making them unlikely candidates as the primary enabler of signal detection.

The SDBs house much of the primary data implying a significant role and new demands will arise as a result. The capturing and structuring of information in ways that enable aggregation are the key drivers that will influence SDB functionality such as:

- Dictionaries at event and product level with configurable structures supporting multiple aggregation criteria
- Integration with other sources of product and event data within the organization. Product complaint and clinical development systems are frequent sources of event data; product definitions typically have shared responsibility across two or three functions and multiple structures driven by different needs.

These will be the minimum expectation to enable effective signal detection.

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### Ranking within key categories

The functionality and technology categories make up the bulk of the survey questions and five of the top six aggregate rankings are from these two categories.

The top 5 rankings within these categories therefore present five additional significant factors as follows:

- Inability to move towards a more efficient paperless or semi-paperless process
- Query performance
- Discontent with current vendor
- Dictionary management – inability to support/integrate with new dictionary management system
- Vendor no longer provides support for installed version

Query performance refers to tools that enable users to define criteria for extracting data and issues are very similar to those for reporting performance.

Regulations specify many requirements affecting availability/access to original documentation, traceability, document retention, and notification requirements, giving increasing significance to the paperless concept. It combines multiple techniques such as the use of structured, standardized formats, document scanning, character recognition technologies and tracking tools, which if properly interfaced to and leveraged by the SDB functionality within a well-defined process, will facilitate a 'paperless environment'.

As an example, the ability to scan original documentation into electronic format and associate it with a particular case solves the regulatory requirement for access to original documentation by many parties, enables tracking, automates audit trails, reduces probability of errors by capturing the essence of data in 'error-proof' structured formats, ensures case and documents move in unison and of course, eliminates the need for photocopies reducing paper.

### Do the survey results “ring true”?

There is a perception that an increasingly stringent regulatory climate is creating demands that current SDBs will not deliver, causing some observers to forecast a reduction in the life expectancy of SDBs as PVOs resort to more frequent upgrades and replacements to comply with new regulations.

These perceptions are not supported by the survey results which indicate a normal life expectancy and rank only one factor of regulatory origin in the top 5.

The strong trend to deploy COTS solutions over custom is probably an indication that COTS solutions have reached a maturity level that enables them to satisfy the broad commonality across PVO needs. This migration to COTS increases the onus on vendors to keep their systems up to date with current and imminent regulations and may even reduce the pace at which vendors retire support for any particular version.

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The central theme driving regulatory policy is to make patient safety a core value encouraging responsible and ethical behavior corporate-wide in respect of patient safety. This will raise by an order of magnitude the acceptable 'standards' of compliance and will manifest as requirements for new and enhanced functionality rather than as identifiable regulatory mandates such as electronic submissions.

AE processing, expedited and aggregate reporting of high quality will be a basic requirement – an *entry requirement* as it were to the more fundamental and value add responsibilities embodied in signal detection and risk management concepts.

Viewed from this perspective the survey results make good sense. The issues troubling PVOs - reporting and query performance, support for signal detection, workflow automation and paperless environments are the basic functionalities that must be in place for compliance, yet are not yet able to robustly support an environment where the risk component of the risk-benefit equation is coming under closer scrutiny.

This shift of PVO core activities to effective signal detection and risk management. will require PVO's to demonstrate a more *holistic* view of their product safety based on a wider data set than that housed in the SDB. This will drive a need to easily share information across multiple groups including product complaints, regulatory affairs and clinical studies, as well as importing of data from external sources.

To continue to deliver the primary enabling role for PVO's, SDB vendors might anticipate that the next phase of critical needs will be centered on a tighter integration capability with other systems to expand the data set available, and the analysis capability required to transform that data into the safety information and knowledge required for truly effective signal detection and risk management.



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