Introduction

Strategic planning, sourcing and implementation of pharmacovigilance operations are multi-dimensional activities that require consideration of factors across the spectrum. Over the past few years there has been a positive increase in the quality and quantity of safety processes being outsourced. The trend is largely due to evolution of mature processes; risk mitigation strategies and increase in vendor experiences that has helped the sponsor balance core in house strength and leverage the service provider’s capabilities. Though approach towards outsourcing pharmacovigilance is largely tactical, strategic partnership with a vendor is not uncommon.

Sourcing strategy would vary based on sponsor’s product portfolio, therapeutic areas, internal capabilities, expected case volume, expected complexity of cases, geography of product sales and risk management requirements. For
instance, a sponsor might decide to outsource few steps of pharmacovigilance process that the organization classifies as non-critical or might outsource the entire process from case receipt to submission. Sponsor would have to make a series of decisions on their preferred nature of engagement like choosing between a pilot and a permanent contract, migration to steady state, vendor management, KPIs (quality, cost, time) and success metrics. This concept paper, based on our proprietary model, discusses facets of a smart sourcing strategy.

Framework for Outsourcing of Pharmacovigilance Operation

Based on years of experience we have evolved a proprietary model and framework that enables our clients to choose the optimal Pharmacovigilance outsourcing partner consistent with their strategic objectives.

We have used this model to help our clients identify the right fit and determine the extent and volume of scale-up leading to a successful outcome of their outsourcing initiative. Offshore support based on this model is currently in steady state and we continue to evolve this model.

Our partner assessment model has been discussed in various industry group meetings and the basis of the model has been validated by practitioners of Pharmacovigilance across the world.

Our assessment framework provides a roadmap to outsourcing PV operations based on maturity of the current in-house process and provides recommendations on partner selection model customized to the specific needs of our clients’ product vigilance process. As a second step, our model provides quantitative measures to plan process transition and key milestones to ensure a successful outcome.

Partner Assessment Model©

Our proprietary framework involves an assessment of the overall pharmacovigilance processes, across three broad categories of service providers: Global CROs, Regional CROs and Large IT companies that offer BPO capabilities. Assessment is performed against six different criteria:

- Operational Capability
- Regulatory Compliance
- Technology
- Team
- Process Maturity
- Business

Figure 1 shows the outcome of an assessment we conducted for one of our clients using our proprietary model. Based on publicly available data, each category was rated across the three different types of service providers mentioned above and was compared with industry benchmarks. The client used this information to formulate their sourcing strategy and Sciformix was awarded the engagement to support their PV operations from our delivery center in Pune, India and Manila, Philippines.
If opting for a risk based approach to outsourcing, a sponsor might want to lower the risk by selecting low.

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**Outsourcing approaches**

We apply our Partner Assessment Model© and Product Vigilance Process Maturity Model© in the context of the client’s approach to outsourcing. Our insightful and customized application of our tools helps our clients make and implement the right decisions.

**Risk-based approach**

If opting for a risk based approach to outsourcing, a sponsor might want to lower the risk by selecting low.
complexity activities, products and activities to be externally sourced. The first step is to clearly determine what can be considered as “low risk” from both the product portfolio from both the product and process complexity perspective.

While this approach might safeguard perceived ‘sacred cow’ in the short term. If one of the objectives for the initiative is to rationalize overall case costs, this approach may not provide the most optimal solution. A reasonably deconstructed process will allow easier transition of perceived ‘low risk’ activities.

**Deconstructed process approach**

A deconstructed process approach allows individual steps within a process to be separately outsourced. For example, it would make it possible to retain case intake and submissions internally or to outsource it separately, and include case entry, coding etc. in the central sourcing strategy. However, the sponsor would be required to invest significant time and effort in standardization of process involved between different vendors initially. In the longer term, the primary role of the sponsor will be to manage the hand-offs between various sourced partners.

**Figure 2: Deconstructed process approach**
Figure 2 shows how a deconstructed process works across multiple providers. The biggest challenge in this approach is to arrive at the optimum level of deconstruction to ensure effective management of hand-offs between various partners.

Since pharmacovigilance is a time sensitive process, a poorly deconstructed and inefficiently handled process manifests itself in late submissions. For example, if the case intake and case processing activities are handled by two different providers, managing follow-up calls becomes very critical. In our experience, for spontaneous AEs, when the process reaches steady state, approximately 30% of the cases reported to the call center require active follow up. If the follow up activity is handled by a different provider, chances of calls being dropped is higher, leading to poor case quality and lower timeline compliance.

The sponsor in this case ends up spending an inordinate amount of time reconciling processes across two different providers. Our tools incorporate this learning and it manifests in the form of weightage that we assign to various factors for the evaluation criteria when we develop an optimal sourcing model for each of our clients.

### Sciformix Approach to Benchmarking and Transition

We have developed a series of measurable and quantifiable metrics which enable us to compare our client’s processes against industry benchmarks and best practices.

**Product Vigilance Transition Index©** provides a recommendation which we flesh out collaboratively with the client team along five defined dimension.

One of the other key outcomes of this assessment is a recommendation for the optimal pace of execution of an outsourcing initiative in the context of managing the associated risk. This is quantitatively captured in the **Safety Transition Index©**.

<table>
<thead>
<tr>
<th>Index</th>
<th>Client Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 – 3</td>
<td>Client’s process and operations are not ready to be outsourced. Recommended steps are to introduce rigor in the existing process through better definition of roles and responsibilities, baseline existing operations for productivity (# cases/ FTE per day) and Quality (% critical, major and minor errors) and re-engineering of existing processes.</td>
</tr>
<tr>
<td>Index</td>
<td>Client Status</td>
</tr>
<tr>
<td>-------</td>
<td>---------------</td>
</tr>
<tr>
<td>4 – 7</td>
<td>Parts of the client’s process are mature to be supported from an outsourced provider. Understand hand-offs and dependencies between what is retained and what can be supported from an external provider, what level of oversight is required to ensure continuity in operations, mitigation factors for commonly encountered risks (e.g., definition of Day 0) for activities considered for outsourcing. Better defined parts of the process which are not as mature (e.g., safety data exchange agreements, updating CCDS, centralizing product registry information across geographies) and baseline these activities.</td>
</tr>
<tr>
<td>8 – 10</td>
<td>Client’s process is mature to be supported by an external provider. Create expected Service Level Agreements based on current baseline, formalize the rate of outsourcing activity (how much work to be supported by an outsourced provider and how soon), evaluate portfolio segmentation, perform product risk categorization and develop a 3-5 year projection for an outsourced operation.</td>
</tr>
</tbody>
</table>

Sciformix approaches transitioning PV processes from its client’s locations to its operational centers based on factors like client portfolio size, portfolio maturity and volumes. The approach depends on the ability for the client’s team to expend focused time and effort and financial objectives of the sourcing and urgency in achieving them.

The approach could be one of the following:

**Big Bang Approach**
The transition of operations is completed in one shot.

**Wave approach**
Processes is transitioned in multiple waves over a longer period of time and the approach would be product, function and geography specific.
Figure 3: Sciformix Transition Approach

**Goal**

1. Formalize process to establish a robust pharmacovigilance infrastructure (people, processes and technologies)

**Key Activities**

1. Current process review
2. Current systems review
3. Organization and people/competencies review
4. Redesign processes and develop detailed prerequisites (eg SOPs, training, systems, KPIs)

**Phase 1: Planning**

- Transition Processes and Roles and pilot the process
- Redefine roles, responsibilities and authorities globally and locally to support vision and processes- redesign organizational model
- Contingency planning
- External environment changes

**Phase 2: Transition**

- Initiate performance measurement
- Train off-shore resources
- Initiate communication/change management program
- Create framework to enable continual process improvement in response to environmental changes

**Phase 3: Steady State**

- Identify opportunities for improving process efficiency through process reengineering and IT intervention.
- Initiate process audits to identify opportunities for process improvement
- Deploy process improvement methodologies to improve quality, productivity and reduce Turn Around Time
- Deploy IT tools like macros to reduce manual intervention and increase process efficiency

**Continuous Improvement**

Execute processes in-scope consistent with the SLAs agreed.
Key components of Steady State Operations normally include:

**Processes**
- Operation in “predictable” mode: Processes will be well documented with all scenarios covered by work instructions.
- Process executes seamlessly across functions and locations and Hand-offs between the client and Sciformix are well understood and smooth.

**People**
- Team is trained and certified on the processes.

**Continuous Improvement**
- Weekly global team review by selecting and dissecting sample cases processed in the previous week.

**Volume**
- Predictability and meeting SLAs

**Quality**
- Guaranteed compliance with regulatory requirements
- Robust QA and feedback mechanism
- QA level reduces gradually to stabilize at ~10%. If quality levels are not met then QA level is successively increased.
- Quality and regulatory compliance, feedback mechanism
## Figure 5 – Monitoring Process at steady State

<table>
<thead>
<tr>
<th>Strategic goal</th>
<th>Strategic Metrics</th>
<th>Strategic Sub-Metrics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compliance</td>
<td>% of cases submitted on time to health authorities</td>
<td>% of cases validated on-time by due date (e.g., 4 day, 12 day)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>% of cases submitted on-time by due date (e.g., IND-7 day, IND-15 day, NDA-15 day) by HA region (e.g., FDA, EMEA, Lat-Can, Asia-Pac, etc)</td>
</tr>
<tr>
<td>Operational Excellence</td>
<td>Cost: Average cost per case processed</td>
<td>Average cases processed per FTE by process step</td>
</tr>
<tr>
<td></td>
<td>Productivity: % of single cases processed within X business days of case creation</td>
<td>% cases finishing QC within 5 business hours, 10 business hours, 2 business days, or 3 business days of case creation</td>
</tr>
<tr>
<td></td>
<td>Quality: % error rate, Drug Safety Committee</td>
<td>% cases validated within 1, 2, 3 or 5 business days of case</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Average time by process step</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Thresholds for critical, major and minor error categories</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Feedback from DSC and Regulatory Agencies</td>
</tr>
<tr>
<td>Non-strategic key metrics</td>
<td>Volume</td>
<td>Cases received (e.g., by origin, by version, by nature, by product &amp; location)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cases validated</td>
</tr>
</tbody>
</table>
**Metrics and SLAs**

The table below is a representative set of steady state KPIs. We work collaboratively with our clients to tailor these KPIs to their specific needs during the planning discussions at the beginning of the engagement.

<table>
<thead>
<tr>
<th>SLA Category</th>
<th>KPI</th>
<th>Measurement</th>
<th>Target Service Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Performance</td>
<td>Turnaround Time</td>
<td>Submission to client by Day 3 for SAEs</td>
<td>100%</td>
</tr>
<tr>
<td>Quality</td>
<td>Error Rate</td>
<td>Percentage of critical or major errors detected per quarter</td>
<td>&lt;2%</td>
</tr>
<tr>
<td>Timelines</td>
<td>Regulatory Compliance</td>
<td>Percentage of cases submitted on time to regulators</td>
<td>99%</td>
</tr>
<tr>
<td>Volume</td>
<td>Productivity</td>
<td>Number of SAEs reviewed or completed/data reviewer on a 4 week rolling average</td>
<td></td>
</tr>
</tbody>
</table>

PV processes are fundamentally different from processes like Data Capture and Discrepancy Management. The process of triage, case entry and medical coding is much more complex and subjective. Further, label and causality assessment requires years of training in understanding the mechanism of action of the drugs.

Since we provide end-to-end support for Pharmacovigilance operations, we have developed a better understanding of how individual case assessments shape the aggregate analysis reported in a PSUR or a PADER, how EU RMPs and US REMS evaluate the overall risk of the product in the market and how case processing and aggregate report authoring activities enable effective management of overall risk-benefit balance for the products we support. Our approach balances process rigor, flexibility and adaptability to provide our clients with an optimal pharmacovigilance solution.

Sciformix provides access to a team of experienced therapeutic area Key Opinion Leaders (KOLs) and Subject Matter Experts (SMEs) across our service delivery centers in India and US. Our delivery model provides us the ability to scale up or scale down depending upon the evolving needs of our client's product portfolio along with cost effective services delivery enabled by leveraging a globally distributed team.

Our proprietary tools and methodologies enable us to increase the probability of success of an outstanding initiative for our clients by leveraging our experience, industry benchmarks and best practices in Pharmacovigilance operations.