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WHITEPAPER

From GCP to GVP:
A Pharmacovigilance Guide for Emerging Biotech Firms

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EXECUTIVE SUMMARY

Transitioning from clinical development to post-marketing represents a critical phase for emerging biotech companies, demanding the establishment of robust pharmacovigilance (PV) systems. Given the resource and expertise constraints often faced by smaller biotech firms, outsourcing to Contract Research Organizations (CROs) emerges as a viable solution. However, this approach introduces its own set of challenges, including maintaining control, ensuring quality, and managing flexibility.

This whitepaper explores strategic considerations and practical steps to optimize PV activities outsourcing. It aims to guide biotech executives through the challenges of selecting operating models that align with their company's objectives, regulatory demands, and market dynamics. The paper discusses the balance between leveraging external expertise and retaining crucial oversight of PV operations.

Key insights include:

- The significance of delineating core from non-core activities to ensure strategic oversight remains in-house, while operational tasks can benefit from the expertise and scalability of external providers.
- The strategic selection of CRO partners, emphasizing the importance of alignment beyond cost considerations to include expertise, quality, and operational compatibility.
- The crucial role of ongoing management and quality oversight to maintain compliance, data integrity, and the ability to adapt to emerging challenges.

These considerations allow biotech companies to manage effectively the balance between external collaboration and internal control. This ensures not only regulatory compliance and patient safety but also positions the company for sustained growth and resilience in the competitive biotech landscape.

INTRODUCTION

Small emerging biotech companies face the challenge of moving from the late clinical stage to post-marketing operations. Among others, that includes the area of post-marketing pharmacovigilance.

This transition is crucial as they are getting close to potentially launching their product but don't yet have systems in place for monitoring drug safety in a post-marketing setting. In most cases, the still small companies do not have in-house capacities or even the right skillset to create a proper PV system from scratch.

For that reason, companies often turn to large CROs for advice and for taking over the operational burden. A large-scale outsourcing approach can be very attractive as priorities may lie in other important and usually urgent areas and the desire to cover this in-house is usually very low.

However, relying completely on outside help brings its own set of challenges. Companies need to balance flexibility, cost, risk, and opportunity here. How much control do they want to retain and what should the operational structure look like?

The whitepaper aims to discuss the transition process, different operating models, and nuances of outsourcing within biotech, highlighting the delicate balance between leveraging external expertise and retaining essential control over PV operations. It presents a helpful guide for biotech executives, to structure the thought process of building the right operational structure.

CHALLENGES AND STRATEGIC DECISIONS DURING THE TRANSITION

Transitioning from a GCP-focused clinical development stage to a GVP-driven post-marketing phase is a challenge that hinges on strategic decisions around the operating model for pharmacovigilance activities. This transition requires not only a shift towards comprehensive safety monitoring but also a critical evaluation of how to structure the post-marketing surveillance operations to ensure efficiency, compliance, and scalability.

The most notable shift is the expansion of the drug safety horizon from what it was in the distinct clinical setting. The post-marketing PV system expands beyond the R&D barrier well into other fields like commercial activities.

Table 1 Differences of a CCP to a GVP focused organization. While both perspectives can exist in the same company, the transition process can be challenging.

Aspect	GCP-Focused Company (Clinical Development)	GVP-Focused Company (Post-Marketing)
Primary Aim	Prove safety and efficacy in controlled environments.	Monitor safety profile and manage risks in the general population.
Data Collection	From clinical trials, under controlled conditions.	From a wide range of real-world sources (HCP reports, consumer feedback).
Analysis Focus	Efficacy and safety, based on controlled trial data.	Adverse effects, long-term safety, and drug interactions based on real-world evidence.
Regulatory Interaction	Detailed submissions of clinical trial data and protocols for drug approval.	Reporting adverse events, safety updates, and implementing risk management measures.
Stakeholder Engagement	Primarily with clinical researchers, trial participants, and regulatory bodies.	Broader, including healthcare professionals, patients, patient groups, and the public.
Key Activities	Conducting and monitoring clinical trials, ensuring ethical considerations.	Vigilant monitoring for adverse events, communicating risks, and ensuring safe drug use.
Ethical Considerations	Informed consent, participant safety, trial integrity.	Drug safety, public health implications, risk communication.

Managing non-PV vendors, such as sales teams or healthcare professional (HCP) facing service providers, plays a critical but often underappreciated role in the pharmacovigilance system.

Determining the optimal operating model - whether to manage pharmacovigilance activities in-house, outsource to Contract Research Organizations (CROs), adopt a hybrid approach, or explore options like labor leasing - is a strategic decision that impacts the organization's agility, control over pharmacovigilance processes, and ultimately, the ability to ensure patient safety.

Table 2 Comparison of different sourcing models for GVP operations. The details of the different models can vary based on the individual setup. All of them require a solid strategic decision and risk management.

Model	Benefits	Challenges	Level of Control
In-House	Direct control and integration with existing processes and culture.	Significant investment required in infrastructure and expertise.	High - Complete control over activities and decisions.
Outsourcing to CROs	Access to specialized knowledge and scalable resources. Adaptable to fluctuating workloads and regulatory changes.	Coordination and quality oversight can be challenging.	Low to Moderate - Dependent on the CRO for execution, with oversight from the company.
Hybrid	Combines the control and integration of in-house models with the flexibility and scalability of outsourcing.	Managing seamless operation between in-house and external teams.	Moderate to High - Core activities are controlled internally, with selected outsourcing.
Labor Leasing (Staff Augmentation)	Flexibility to enhance in-house team with external experts temporarily, without long-term commitments.	Integrating leased staff into existing teams and processes needs careful management.	Moderate - Increased control over specific tasks or projects, while leveraging external expertise.

This strategic choice must align with the company's size, expertise, budget, and long-term vision for its pharmacovigilance system. It's essential to evaluate each model's implications on the quality of safety monitoring, regulatory compliance, and the capacity to manage large volumes of data and adverse event reporting efficiently.

Integrating strategic thinking with a clear understanding of operational capacities and regulatory expectations is crucial to undergo this transition successfully, ensuring that the focus remains on patient safety throughout the drug's lifecycle.

THE OUTSOURCING DECISION AND ITS CONSEQUENCES

For growing biotech companies, creating a heavily outsourced PV organization is a double-edged sword. On the one hand, it offers access to essential resources and expertise, crucial to cover all requirements without building a large internal overhead. There might also be an existing close relationship with a CRO from the clinical phase that makes a continuation for post-market activities more attractive.

On the other hand, the scaling of such structures comes with risks and challenges that may take years to become visible but can create a lot of headaches as well as unpredicted cost.

In contrast to the early days, there are now many factors beyond cost that are relevant considerations in the outsourcing decision (DeCorte, 2020):

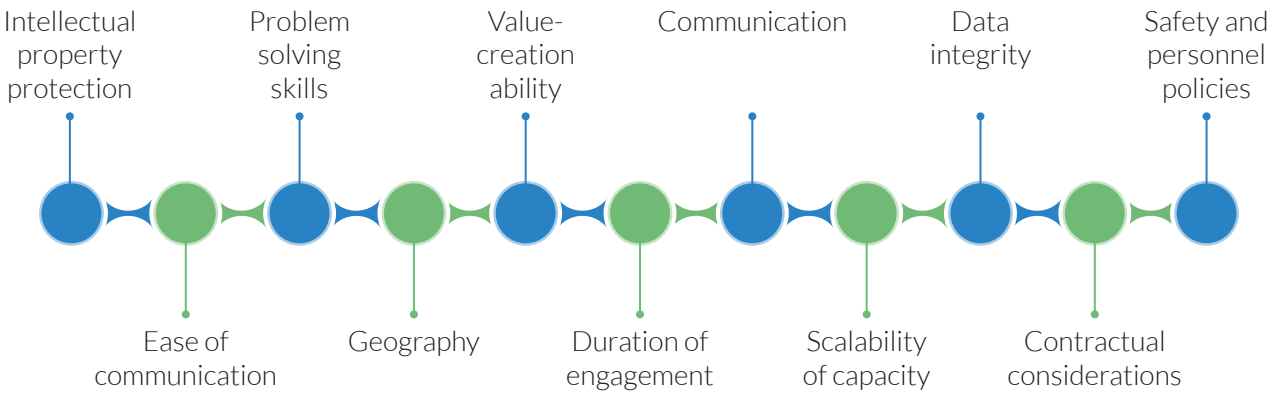

Figure 1 *Different considerations for outsourcing decisions beyond cost-saving. Based on DeCorte, 2020*

There are in fact some documented cases where keeping PV in-house has been perceived as advantage, emphasizing improved oversight, data quality, and faster responses (Kim, 2024).

COMMON CHALLENGES

Imbalance

One primary concern is the imbalance of power. Large CROs cater to numerous clients, including some of the biggest names in the industry, which might lead to smaller companies feeling deprioritized. This can manifest in longer response times, less flexibility, and sometimes, a sense that their specific needs are not being fully addressed.

In addition, negotiating terms that protect the biotech's interests becomes harder in this unequal relationship. Small companies may struggle to secure favorable contract terms or assert their needs in project timelines and milestones.

This situation is further complicated by the significant dependency on these outsourced partners for critical development functions, from clinical trial management to regulatory submissions.

Quality and Oversight

Moreover, the challenges of managing these partnerships demand a high level of oversight and coordination, which in turn can stretch the limited resources of a small biotech even thinner. The fear of losing control over their own operations is palpable. A lack of experience and knowledge may leave the sponsor vulnerable to deficiencies of the CRO (Peterson et al., 2021) or at least it makes it difficult to monitor.

Strategic Decision and CRO selection

Despite the challenges, the reality is that small biotech companies must master this situation to progress. It requires a strategic approach to selecting CRO partners, creating the appropriate operational structure and being able to scale.

It may often be the case that the sponsor organization doesn't have the right resources or skills to manage the outsourcing process in a proper way.

THE IMPORTANCE OF THE RIGHT OPERATING MODEL

"Just handing over" the entirety of operations to a Contract Research Organization (CRO) is most certainly a mistake for biotech companies, particularly when dealing with the critical transition from late-stage clinical trials to post-marketing pharmacovigilance. The right operating model involves not just selecting a competent CRO but also defining what operations and responsibilities should be outsourced and what should remain in-house as strategic core competencies.

Maintaining control

Total reliance on a CRO can lead to the sponsor company losing control over critical aspects of its operations. This can make it challenging to ensure that the project aligns with the company's priorities and regulatory obligations. Regulators require evidence that the sponsor still retains an appropriate level of control over their drug safety operations even when outsourcing it to a partner. The accountability remains with the Sponsor. It is especially true when it comes to the heart of the safety organization: *The Safety Database*. Fortunately, the current cloud-based safety systems allow maintenance of operational control and oversight regardless of the general outsourcing model and the selection of a specific operational service provider (Kim, 2024).

Flexibility and Responsiveness

Companies under development might find themselves less able to quickly pivot or respond to emerging data, regulatory feedback, or market changes when all operations are managed externally. There might even be a high level of dependency that leads to lack of power dealing with quality issues, especially if the CRO is also the technical host of the safety database. The latter could even prevent a necessary change of service provider, creating a "locked-in situation".

STRATEGIC COMPONENTS OF THE OPERATIONAL MODEL

Core vs. non-core Activities

There are activities that are core to the company's strategic objectives and those that are supportive or supplementary. Core activities often benefit from remaining in-house and/or under close supervision, while non-core activities can be more efficiently handled by external service providers.

Table 3 Example of a high-level distinction of core vs non-core activities. It must be clear that the results of the considerations can be very different based on the organization and product portfolio. Even for core activities, external expert support in an advisory role can be needed.

Activity Type	Specific Activities	Management Approach	Rationale
Core (Critical)	• Signal detection • Risk Management • Plans (RMPs) • Benefit-risk assessment	In-house/close supervision	Critical for compliance and competitive edge. Requires deep knowledge, quick decision-making, and strict quality control.
Core (High Expertise Required)	• Regulatory strategy and submissions • PV system design and updates • Compliance audits and inspections	In-house/close supervision	Integral for strategic direction, regulatory alignment, and maintaining high compliance standards.
Non-Core (Routine)	• Case processing • Data entry and database management • Literature review for case reports	Outsourcing	Operational tasks that can be standardized and do not require strategic decision-making. Cost-effective and scalable.
Non-Core (Supportive)	• Training materials development • Software maintenance for PV databases • Translation services for global reports	Outsourcing	Support functions that benefit from specialized skills not central to core PV competencies. Allows for flexibility and efficiency.

Expertise and Specialization

Outsourcing in general should be strategic about leveraging the specialized expertise of CROs, especially in areas where the sponsor organization may lack depth, such as specific regulatory knowledge or advanced data analytics for pharmacovigilance. Another important consideration is the sourcing of expert capabilities that are not required in a full-time capacity or only periodically.

Scalability and Flexibility

The ability to scale operations up or down based on the development phase and market needs without incurring prohibitive costs or delays should be a key consideration. The COVID-19 pandemic underscored the need for companies to include pandemic preparedness in their strategic planning and risk mitigation efforts. It highlighted the importance of planning for redundancy and backup capacity to protect against unanticipated events and ensure business continuity. In addition, considerations on redundancy and disaster recovery need to be part of the risk assessment (Beninger et al., 2022). All this feeds directly into a sound operating strategy.

RISKS OF AN OPERATING MODEL THAT RELIES ON OUTSOURCING

There are some general risks associated with the outsourcing process that can be mitigated. Key is to find an appropriate balance between cost-pressure and risk. It is important to note that accepting a risk sometimes only postpones cost to the future.

Misalignment on quality standards and regulatory requirements can result in data integrity issues, audit findings, and potential market access delays.

To mitigate those risks appropriate vendor management and quality management needs to be in place with the sponsor (!) organization. It is not sufficient, to leave quality management in the hands of the service provider.

For a critical PV vendor, the qualification standards need to be the highest and due diligence needs to be performed.

Table 4 Different sourcing strategies come with different risks that need to be aligned with the organizations risk appetite and priorities

Risk	Potential Risk Mitigation Strategy
Quality issues	• Quality Management System • Vendor Management • Ongoing Quality Monitoring
Locked-in situation	• Separation of different service areas (e.g. Database hosting vs. case processing) • Utilization of Cloud-Based Safety Systems • Opting for a multi vendor model
Loss of control & Loss of in-house capabilities	• Retaining strategic capabilities in-house • Close involvement of sponsor and transparency on the operational level • Risk-based process management (Planning based on the inspection priorities, published by the regulatory Authorities, i.e. the MHRA (MHRA, 2023))
High cost/Insufficient value for cost	• Appropriate vendor selection process • Contractual design • Setup that addresses a potential locked-in situation

PROPOSED HIGH-LEVEL GUIDANCE FOR AN EXEMPLARY DEVELOPMENT PROCESS OF AN OPERATING MODEL

The following steps aim to provide a high-level guidance on a potential process to get from the clinical stage to the post-marketing PV organization. Please keep in mind that the details heavily depend on the sponsor organization and require an experienced program management team. The scope of the individual steps can vary in terms of effort and required lead time.

1. Define Strategic Goals and Objectives of the Process

- What are the organization's goals in general?
- What does the organization want to achieve with the outsourcing?
- Is there potential for cross functional outsourcing?
- Are there any limiting factors or pressures that will influence the outsourcing initiative?
- What are the financial options and limitations?
- What are the regulatory requirements for the products and target markets?

2. Asses internal Capabilities

- What internal capacities and skills does the organization have or need?
- Are there other corporate functions that can contribute to the outsourcing project? (e.g. corporate procurement, legal, IT)
- Are there existing service relationships in place that are relevant for this process?

3. PV Activities Scoping

- Outline the different operational components.
- Map the components against strategy, objectives, regulatory requirements, and internal capabilities.
- Perform a risk assessment and decide on how to cover the component.
- Make decision on the desired technology setup (e.g. Safety Database)

4. CRO Selection Process

- Perform a selection process based on the collected requirements.
- RFI/RFP/Bid Defense
- Qualification Audit

5. Contract Negotiation

- It may be helpful to engage an external specialized counsel if no in-house resources are available.

6. Onboarding & Implementation

- Technical onboarding
- Operational onboarding
- Setting up quality measures

7. Operational Handover and Continuous Improvement

- Ensure that the vendor is part of the corporate vendor management structure.
- Monitor KPIs and Monitor Quality
- Requalification Audit, if needed

CONCLUSION

Developing an effective operating strategy for pharmacovigilance goes beyond just improving efficiency and managing costs. The key is a strategic approach that encompasses asking the right questions, selecting the right partners, and maintaining strong oversight.

That means:

- **Distinguish Between Core and Supporting Activities:** Decide which PV functions are critical to keep in-house for strategic oversight and which can be efficiently outsourced.
- **Align Outsourcing with Strategic Goals:** Clearly identify how outsourcing fits into the company's broader objectives and complies with regulatory demands.
- **Select Partners Carefully:** Choose a service provider not just based on cost but for their alignment with the company's vision, commitment to quality, and operational compatibility.
- **Ensure Strong Oversight:** Implement effective quality management and oversight processes to guarantee compliance, maintain data integrity, and remain flexible to new developments.

Adopting these strategies enables organizations to manage the balance between using external expertise and keeping necessary control. This approach not only ensures compliance and safety but also positions companies for resilience and growth in a competitive environment.

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With more than a decade in the pharmaceutical sector, Stefan Brüning had the privilege of working on a wide range of projects and collaborating with top-tier organizations. His in-depth understanding of the industry's nuances allows him to provide valuable insights and solutions.

With a proven track record in creating and improving Pharmacovigilance systems, Stefan has helped organizations streamline their processes, enhance their compliance measures, and proactively identify and mitigate risks.

His goal is to make Pharmacovigilance not just effective but also scalable and compliant.

Would you like to know more about improving your PV organization? We would be interested to hear about your challenges.

Book your free introduction call and connect on LinkedIn!

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