

## Putting Safety at the Heart of Supplier Controls

**Marketing authorisation holders' responsibility for ensuring the continuous monitoring of the safety of a medicinal product across the marketing authorisation lifecycle includes accountability for all third party suppliers with a potential impact on that safety profile. Arriello's COO, Anna Lukyanova, provides practical tips for maintaining a robust safety profile through tighter controls right along the supply chain.**

The global Life Sciences supply chain has experienced unprecedented turmoil recently, creating a challenge when it comes to ensuring end-to-end quality and safety. Suppliers could include anyone from local distributors or qualified persons to IT system partners, security providers and even auditors themselves. Increasing changes to suppliers and service providers affect the vendor records and controls companies must maintain to ensure end-to-end quality and safety.

If control issues are exposed during inspections, that could lead to fines, or even product withdrawal from affected markets. Scenarios potentially triggering an inspection could include a distributor failing to flag an effective product recall in a particular market; a local partner failing to implement additional risk minimisation measures (aRMMs); or a local qualified person being unreachable by the relevant authority due to out-of-date contact details or the vendor going into liquidation.

Regulators are expected to issue firmer guidance on vendor management controls sooner rather than later. In the meantime, robust vendor management is an expectation under EU GxP requirements. So, if drug developers or licence holders fall short, they could risk their reputations as well as significant fines and ultimately product withdrawals.

### Start by Creating a Definitive List

To address this issue, it's important to start by identifying ALL suppliers with a potential bearing on a products' safety profile, however

tenuous. Once a definitive list has been compiled, each supplier can be reviewed for potential risk/safety impact and appropriate due diligence. (Ideally, such factors should form part of the risk-based evaluation conducted before entering into a contract with a new supplier or service provider.)

Suppliers range from sales and marketing companies which capture data and could come across adverse events (AEs); outsourced service providers – e.g. of data management; biostatistics; medical writing; pharmacovigilance (PV) service providers; IT providers that host the company's safety database or ensure the safety data being stored; and independent PV or Clinical Safety contract auditors. Then each third party can be assessed for potential safety profile impact, the current supply/contract status and any monitoring, and required next steps.

### Vendor and Quality Management Go Hand in Hand

A robust vendor management system (VMS) is every bit as important as a robust quality management system (QMS). Ultimately it should form an integral part of the QMS, and awareness, training and buy-in to vendor management practices should be formalised with appropriate communication and training.

Governance and the sharing of business decisions with the Safety/Pharmacovigilance Quality Assurance (PVQA) department prior to contract emerge as important, positive practices, too. Additionally, all contractual arrangements with PV agreements, clauses or a PV section should be reviewed by the Safety/PVQA department. MAHs should have all responsibilities clearly documented in an appropriate agreement, to avoid misunderstandings around relative responsibilities.

### Tailor risk-based Questionnaires

It is key to assess the potential impact of any proposed new vendor on the safety profile based on the services it is going to provide. For instance, a third party that is providing services that are critical to the delivery of the safety profile, maintenance, evaluation of the product (e.g. CRO, PV service provider, medical information provider, outsourced clinical services) will require greater vigilance than

one that does not have a direct impact on the safety profile, maintenance or delivery of product and whose failure would not disturb clinical or PV operations.

Suppliers posing a 'significant' if not critical risk, in that their failure could disrupt the business, must be included too. Performing an audit or risk-based questionnaire on all critical and significant third parties is suggested best practice. A templated questionnaire for each service type means this can be sent swiftly to proposed new partners with a timeframe for delivery that minimises any impact on business timelines.

Although the level of initial due diligence required may be determined to an extent by per third-party type, each respective relationship will need to be reviewed in its own right to allow for other variances and influencing factors. A critical or significant lone contractor that uses the company's internal quality system might be made exempt from this type of questionnaire where proof of training, CV, and certification may be deemed adequate, for instance.

Due diligence could take one or more forms, including: risk-based questionnaires based on the contractual obligations of the third party; Pre-qualifications audits; proof of qualification documentation; proof of training and proof of required registrations and relevant certification; and/or references, CVs and interviews.

Once the new partner has been classified, the associated risk level must be assessed through a process of due diligence. The objective here is to gather and review all relevant information to facilitate an informed, risk-based decision as to whether your organisation should enter into a contractual relationship. Performing an audit or risk-based questionnaire on all critical and significant third parties is suggested best practice.

Finally, a third-party score (TPS) is given. The final TPS derived from the due diligence process may identify the need for a pre-qualification audit where not otherwise conducted. While a risk-based questionnaire

should not supersede the need for audit with critical and significant vendors, it may provide justification for the timeline of the scheduled audit.

### Understand the Cut-off Point if Breaches are Untenable

Other potential risk factors may also need to be mitigated through evidential proof of compliance, or potentially via an audit. Only when a potential risk becomes a confirmed risk would a 'for-cause' audit be required, or if deemed appropriate, a review of the vendor themselves to consider the continuation of the contractual arrangement.

All contractual arrangements affecting the safety profile should contain a clause to ensure that, in the event of confirmed non-compliance with evidential proof, the contract can be ended. This is important. Although contract termination is a last resort, the option to end the relationship is paramount to ensure ongoing compliance if so needed.

It is a good idea to keep an eye on the audit programme and ensure it is updated to identify potential and emerging risks. Audit program updates should ensure that changes to the audit cycle are based on potential risk or confirmed risk (for-cause audits), so that all open, potential risks are reviewed during the audit – if not mitigated through other means prior to audit.

Risk-based questionnaires, previous audit findings, and logged potential risks can lead to a better more focused third-party audit and therefore more relevant/detailed findings and better corrective and preventative actions (CAPAs).

Maintaining open, transparent communication with third-party vendors throughout the audit and due diligence program can help pinpoint potential inspection findings internally so that these can be avoided, averting regulatory-led penalties for non-compliance.

### Eight Steps to Safety Along the Supply Chain

1. Advise everyone concerned about the impact of all kinds of third-party suppliers and service partners on safety.
2. Get the Safety team involved in vendor selection due diligence before the contract is signed.
3. Practise ongoing communication and open sharing of information – all



- paramount to a good third-party relationship.
4. Review potential risk factors continuously, to ensure ongoing compliance.
5. Set out respective responsibilities clearly in contracts to ensure there is no misunderstanding of responsibilities around sharing changes to information.
6. Make sure your chosen vendor management system, like a good QMS, reflects the company's organisational complexity.
7. Audits are not the definitive solution to effective vendor monitoring and management. Don't rely on audits to flag changes and issues. Foster good relationships with relevant third parties, and keep re-evaluating them.
8. Support buy-in to supply chain safety management from everyone – from business development and contract management, to marketing and beyond.

### Ongoing Due Diligence

Identify and review any contractual changes made throughout the contract to ensure continued safety. Regular testing of contract details to ensure they are still valid and correct offers one simple way to uncover changes that may not have been identified otherwise through routine process.

From a post-marketing perspective, under GVP Module IV.B.1. (Pharmacovigilance audit and its objective) there must be ongoing due diligence and assessment, alongside an audit program based on risk. This should reflect evolving factors such as changes to legislation and guidance, or a major reorganisation/restructuring of the PV system (e.g. following a merger/acquisition).

Ongoing due diligence should ideally include the maintenance of the initial due diligence documentation (e.g. request a

CV every two years, if certification requires renewal, request renewal); the reporting/gathering of any changes that could impact the third-party risk profile score (TPS); sufficient tracking of potential risks and review of any potential or confirmed risks that change the TPS, and identify mitigations to ensure the TPS is kept within acceptable boundaries. Everyone in the organisation should be aware of the vendors in their ecosystem and should be clear on how to report any changes to safety/PVQA to investigate the potential risk of those changes.

Rigour and consistency are essential at a worldwide level, given the global nature of today's businesses and their supply chains. As authorities globally are closing in on vendor management and working towards more formal requirements, all drug licence holders must take back control of their end-to-end safety profile through robust vendor management.

Find the full Guide 'Vendor Selection & Management: Maintaining a robust safety profile through tighter supplier controls' here – <https://arriello.com/guides-ebooks/vendor-selection-management-maintaining-a-robust-safety-profile-through-tighter-supplier-controls/>



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