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Inspection Readiness in Global Pharmacovigilance: Lessons from FDA, EMA, and MHRA Regulatory Expectations

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Abstract: Inspection readiness is a core organisational capability for marketing authorisation holders and equivalent FDA-regulated application holders in the US, EU/EEA, and UK markets. It is not only about readiness for the next inspection, but also about routine management of safety information, governance, signal detection, risk minimisation, vendor management and traceability of evidence to support pharmacovigilance decisions. This review examines peer-reviewed literature since 2015 that contributes to inspection readiness, including regulatory intelligence, quality of safety databases, patient safety reporting, social media, real-world data, artificial intelligence and risk minimisation. The review shows a gap between the abundant research on pharmacovigilance methods and the paucity of evidence from inspection experience, categories of inspection observations, and maturity of readiness. FDA, EMA and MHRA expectations of timeliness of case processing, valid safety assessment, documented quality systems and corrective action can be harmonised for inspections, but the research literature focuses more on technical surveillance methods than on pharmacovigilance quality systems and inspection evidence. Further research is needed for comparable measures of inspection readiness, maturity models and empirical research on the impact of digital systems on inspection readiness.

Keywords: Corrective action; global pharmacovigilance; inspection readiness; regulatory expectations; safety surveillance.

INTRODUCTION

Global pharmacovigilance inspection readiness is an organisational capability to demonstrate, at any point in time, that the pharmacovigilance system is comprehensive, controlled, evidence-driven, and supportive of public health. For FDA, EMA and MHRA inspections, inspection readiness is more than just ensuring documents are available on the eve of inspection. It includes case acceptance, processing of individual case safety reports, signal management, aggregate risk management, risk minimisation, QPPV/responsible person oversight, affiliate oversight, vendor oversight and maintenance of data integrity and corrective and preventive action (CAPA). Since 2015, the peer-reviewed pharmacovigilance literature has progressively shifted the concept of medicines safety from reporting to a systems function because medicines safety governance is enabled by the ability to transform safety information into timely, documented and scientifically defensible decisions *[Beninger, P. 2018]*. This is important for inspection readiness because inspections typically assess the pharmacovigilance system's capacity to document decisions, prioritise activities and manage risks.

The global relevance of inspection readiness has increased because medicines are authorised, distributed and monitored in different regulatory jurisdictions with different legal frameworks, but harmonised expectations for medicines safety. Literature with an EMA focus has emphasised the evolution of pharmacovigilance capabilities under the European legal framework such as centralised reporting, risk mitigation and systemwide accountability *[Borg, J. J. et al., 2015]*. Literature focusing on the FDA has highlighted the shift from passive postmarketing surveillance to active surveillance through Sentinel and other real-world evidence networks *[Ball, R. et al., 2016]*. Further commentary on Sentinel as a national infrastructure also highlighted the importance of considering data provenance, analytic reproducibility and governance of distributed evidence networks, in addition to fast reporting, when considering inspection readiness *[Platt, R. et al., 2018]*. Although there is less peer-reviewed literature about inspection specific to the MHRA than there is about the EMA and FDA, the United Kingdom is still of great interest given that MHRA requirements continue to focus on documented control of the pharmacovigilance system, national reporting systems, risk-based inspection strategies, and governance of post-authorisation safety.

The state of the science is interdisciplinary because inspection readiness in international pharmacovigilance encompasses regulatory science, quality management, pharmacoepidemiology, information management, clinical safety and organisational science. Research has evolved from spontaneous reporting only to capture a wide range of patient reports, health-care professional reports, literature cases, social media messages, electronic health-care data, and structured analysis of regulatory intervention

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and risk reduction. At present, patient reporting is important for inspection readiness because it expands the evidence for safety and provides diversity in narrative data, confirmation of medical diagnosis, seriousness assessment, duplication assessment and causality assessment *[Inácio, P. et al., 2017]*. Therefore, an advanced pharmacovigilance system must demonstrate that broadening the capture of source information does not affect the consistency, timeliness and auditability. For FDA, EMA and MHRA inspections, this means that innovations in safety monitoring need to be tied to rigorous processes, validated systems and published science.

A key issue is that there is little published peer-reviewed evidence on pharmacovigilance inspection readiness. The literature mainly relates to the areas inspected, such as signal detection, database transparency, patient reporting, risk minimisation, real-world evidence, and digital monitoring. There is limited research on inspection outcomes, major inspection observations, reasons for non-compliance and long-term changes following corrective and preventative action. This creates a gap between inspection practice and published pharmacovigilance research. As a result, review articles on inspection readiness draw on research of other, but key, functions. This is appropriate when the function is inspected, but it also calls for caution because tool performance does not equate to compliance.

This article presents a review of how peer-reviewed papers published since 2015 inform inspection readiness in global pharmacovigilance, and more specifically, lessons that can be learnt for compliance with US Food and Drug Administration (FDA), European Medicines Agency (EMA) and Medicines and Healthcare products Regulatory Agency (MHRA) inspections. This article reviews contextual information, compares research approaches, reviews findings and proposes a topic-specific model of readiness as a system of controls. The review identifies gaps in evidence such as the absence of comparative inspections, public reporting of inspection finding typologies, and digital readiness indicators. This article suggests that inspection readiness should be understood as a continuous evidence-control function.

LITERATURE REVIEW

Five clusters of literature relevant to inspection readiness in global pharmacovigilance can be identified: transparency of regulatory systems, patient and public reporting, risk minimisation and evaluation of regulatory intervention, digital and social media monitoring, and governance of analytical processes for large safety datasets. These are relevant to inspection readiness because each cluster relates to an area in which regulators expect safety information to be collected, assessed, escalated and documented with sufficient control. Postigo and colleagues discussed EudraVigilance as a public safety database and the need for structured access to adverse reaction information for research and safety *[Tobaiqy, M. et al., 2021]*. This research is pertinent to EMA-focused inspection readiness because EudraVigilance is not just a database; it establishes a transparent regulatory environment that reveals aspects of reporting quality, data submission, coding, duplicate reporting, and detectability of signals outside of the company's walls. Consequently, inspection readiness requires the internal data to be able to stand up against the external data.

The second major cluster in the literature is that of patient reporting and this has direct relevance to readiness for FDA, EMA and MHRA inspections. Banovac and colleagues examined patient reporting in Europe demonstrating that patient-reported safety data contribute new information to pharmacovigilance databases *[Banovac, M. et al., 2017]*. The study by Inácio et al. also showed that patient reports contribute information that might be missing from reports by health professionals, particularly relating to patient experience, treatment burden and seriousness *[Inácio, P. et al., 2017]*. The inspection-readiness lesson is two-fold. Increased sources enhance signal detection, patient-centred surveillance and reporting, but greater diversity of sources also means increased need for reconciliation, de-duplication, medical review, seriousness evaluation and documented triage. A company cannot be ready just because it knows more about safety; readiness is about safe interpretation and action.

Risk minimisation and regulatory intervention studies best demonstrate a link between pharmacovigilance and public health impact. Vora and colleagues examined studies assessing the effectiveness of risk minimisation actions in Europe via the European Union electronic Register of Post-Authorisation Studies and observed that methods for evaluating effectiveness were diverse *[Vora, P. et al., 2018]*. Goedecke and colleagues also addressed this problem by looking at the measurement of regulatory interventions and the key challenges in attributing changes to regulatory

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intervention *[Goedecke, T. et al., 2018]*. For inspection readiness, this is important as FDA, EMA and MHRA requirements increasingly demand proof of risk minimisation actions being not just recorded but being monitored. A risk minimisation plan without effectiveness evaluation may create documentation but lacks a public-health feedback loop.

Electronic and digital sources expand the pharmacovigilance evidence base. Sarker and colleagues reviewed social media data for pharmacovigilance and outlined the promise of computational methods for adverse event detection of alternative data sources *[Sarker, A. et al., 2015]*. Pierce and colleagues assessed the ability of social media monitoring on Facebook and Twitter to uncover recent FDA safety alerts and offered a more practical test of the effectiveness of social media monitoring for regulatory safety concerns *[Pierce, C. E. et al., 2017]*. Caster and colleagues, in WEB-RADR, evaluated broad-based statistical signal detection of social media, concluding that the practical utility of signals was limited by the noise, lack of clinical details and difficulty in separating adverse event reports from casual conversations *[Caster, O. et al., 2018]*. These studies temper inspection-readiness stories that presume digital growth is automatically beneficial. For inspectors, it is not enough to know if a company monitors all possible online sources, but whether that company has justified its choices, applied processes consistently, and provided explanation of limitations.

The content of individual safety reports also features as a readiness factor. Rolfes and colleagues found important differences between adverse drug reaction reports from patients and health-care professionals *[Rolfes, L. et al., 2015]*. Trifirò and colleagues called for a shift from big data to smart data in pharmacovigilance and recognition of the value of quality, fitness for purpose, and interpretability along with volume *[Trifirò, G. et al., 2018]*. Caster and colleagues studied disproportionality analysis in small databases or subsets and provided tips to reduce false-positive associations *[Caster, O. et al., 2020]*. This body of evidence suggests a balance of volume, quality, proportionality, and documented scientific decision making is needed for inspection readiness. A pharmacovigilance system with a high volume of poorly managed inputs may be busy but it will be vulnerable if the evidentiary trail (from source to decision) is flawed.

Table 1. Summary of key findings

Ref	Focus	Key Findings
[Tobaiqy, M. et al., 2021]	Public pharmacovigilance database transparency and structured access to safety information.	Centralised safety data access strengthens external scrutiny, supports signal exploration, and raises inspection expectations for internal-external data consistency, coding discipline, and traceable submission histories.
[Banovac, M. et al., 2017]	Patient reporting contribution within European pharmacovigilance.	Patient-originated reports add experiential detail and may identify burden or seriousness dimensions not visible in professional reports, but such reports require robust triage, duplicate detection, and medical review controls.
[Vora, P. et al., 2018]	Evaluation of risk minimisation measures using post-authorisation study records.	Effectiveness studies often vary in design, endpoint selection, and implementation measurement, creating difficulty for inspection assessment of whether risk minimisation controls produce verifiable safety improvement.
[Goedecke, T. et al., 2018]	Measurement of regulatory intervention impact.	Regulatory action evaluation remains methodologically fragmented, and causal attribution is weakened by secular trends, co-interventions, and inconsistent outcome definitions.
[Sarker, A. et al., 2015]	Social media data as a pharmacovigilance source.	Digital public discourse offers potential early safety insights, but unstructured language, incomplete case elements, and uncertain exposure information limit direct regulatory actionability.
[Pierce, C. E.	Social media monitoring	Social media sources can identify some safety discussion

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et al., 2017]	compared with FDA safety alerts.	but do not reliably replace structured surveillance systems, making validation and procedural justification critical for readiness.
[Caster, O. et al., 2018]	Broad-ranging statistical signal detection in social media.	WEB-RADR findings indicate high noise and limited routine signal-detection utility, supporting risk-based digital monitoring rather than indiscriminate source expansion.
[Rolfes, L. et al., 2015]	Differences between patient and healthcare professional adverse reaction reports.	Report sources provide complementary information, but variable clinical completeness affects coding reliability, follow-up needs, and inspection assessment of case quality.
[Trifirò, G. et al., 2018]	Healthcare databases and emerging sources for smart pharmacovigilance.	Large data sources improve surveillance potential only when governance, data fitness, analytic validity, and interpretability are established before regulatory reliance.
[Caster, O. et al., 2020]	Disproportionality analysis in small databases or subsets.	Statistical signal detection requires careful false-positive control, especially for sparse data, subgroup analyses, and exploratory signal workstreams subject to inspection review.

In these studies, the greatest advances are in the extension of the pharmacovigilance evidence sources and in the recognition that the governance of medicines safety needs to be evident and not implicit. The literature supports the notion that inspection readiness should not be a static set of bound procedures but a collection of dynamic controls that link data collection, scientific analysis, regulatory response and improvement. But the same literature shows a common weakness. Research frequently focuses on the effectiveness of information sources or analysis techniques without showing how they are integrated into corporate quality systems. For instance, a study might reveal that social media has weak signal, but that does not necessarily convey how an inspector would assess a firm's procedure for social media screening.

Another paradox is that between innovation and compliance. Electronic surveillance, artificial intelligence, real-world data and patient reporting are often touted as ways to improve safety monitoring. However, readiness for inspection can be diminished when new methods exceed procedural control, training, validation and documented decision rules. The expectation of FDA, EMA and MHRA generally is risk-based proportionality, but that proportionality is predicated on a rationale. The literature therefore favours conservatism: innovation enhances readiness only when governance development keeps up with technical development. This is an important message for multinational organisations because global pharmacovigilance systems can involve centralised processing centres, regional subsidiaries, vendors and local reporting requirements.

METHODOLOGY

The key to understanding inspection readiness in global pharmacovigilance is to connect FDA, EMA and MHRA expectations to operational controls to evidence assets to inspection proof. FDA, EMA and MHRA expectations are not the same in statutory language or text but are similar in terms of inspection scope. Companies must show they process all safety data, in a timely fashion, scientifically, escalate data as appropriate and implement risk mitigation strategies (as appropriate). The literature supports the layered approach as research does not typically speak directly to inspection readiness but does evaluate layers that are inspection evidence. Literature on database transparency speaks to submission traceability *[Tobaiqy, M. et al., 2021]*. Literature on patient reporting speaks to source heterogeneity and follow-up discipline *[*Banovac, M. *et al.*, 2017]. Risk minimisation literature speaks to effectiveness monitoring *[Vora, P. et al., 2018]*. Electronic (e-)surveillance literature speaks to method validation and source justification *[Caster, O. et al., 2018]*. The signal detection literature speaks to proportionality and false positives *[Caster, O. et al., 2020]*.

The literature includes systematic reviews, descriptive database studies, comparative report-quality reviews, computational reviews, empirical social media studies, statistical method evaluations and conceptual reviews of automation. Bate and Hobbiger proposed that artificial intelligence and practical automation can only help achieve

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medicine safety if automation is aligned with human decision making, information transparency and quality control *[Bate, A., & Hobbiger, S. F. 2021]*. Karimi et al reviewed text and data mining methods for adverse drug reaction identification and showed the technical performance of these methods has to do with linguistic uncertainty, entity recognition and separating adverse events from other medicine-related issues [Karimi, S. *et al*., 2015]. These methods are relevant to inspection readiness because authorities will not only want to know if a system is available but will want to know if the results are reliable, explainable, verifiable and relevant to safety.

Strengths of systematic reviews are in showing diversity of pharmacovigilance interventions and data sources. But systematic reviews offer generalised results and not operational thresholds for inspection readiness. Descriptive studies of database data shed light on report counts, source types and field completions, but don't necessarily reveal the causes of data quality issues. Computational studies address speed and scalability, but inspection readiness includes change management, system validation, competence and audit trails. This disconnect between study and inspection accounts for the lack of a model of inspection readiness. Most published work is on pharmacovigilance science, but inspectors audit pharmacovigilance systems.

Figure 1 is a model of inspection readiness as a control system. It shows the link between expectations of FDA, EMA and MHRA, global pharmacovigilance quality system, operational control, assets of evidence and inspection story. This figure is not meant to depict a typical process flow, but the vertical connection between regulatory expectation, system control and evidence assets for inspection.

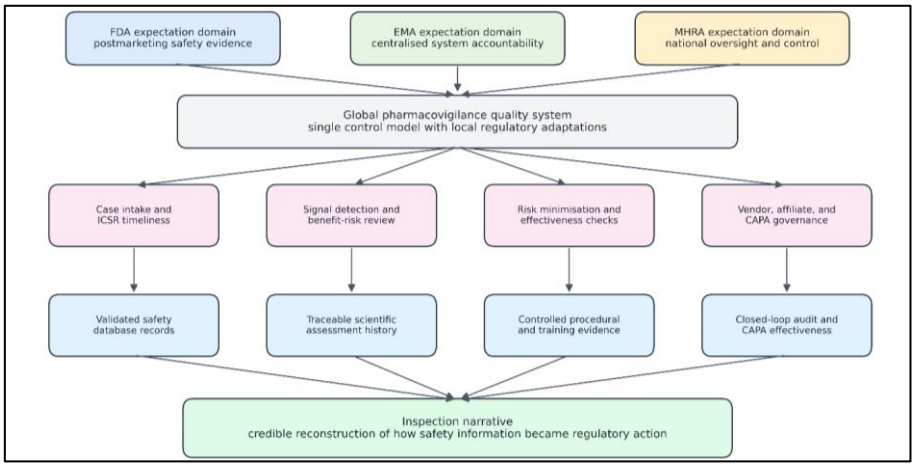


Figure 1. Layered control architecture for inspection readiness in global pharmacovigilance

The figure illustrates the most important point - inspection readiness is an architecture of accountability, not a document set. It also illustrates the need for a governance perspective in research on patient reports, electronic monitoring and statistical triggering. A method with good analytical characteristics is not inspection-ready until the organisation can show ownership, method validation, procedural control, exception management, and corrective-action learning.

DISCUSSION

The reviewed studies suggest inspection readiness is best achieved when pharmacovigilance systems can accommodate multiple sources of evidence to improve decision-making while controlling for quality, traceability and decision-making. EudraVigilance transparency studies support the notion that transparency places pressure on companies to be accurate with their reports, and internally and externally consistent [Tobaiqy, M. et al., 2021]. Patient reporting studies demonstrate that more source capture increases the interpretability of safety signals but increases the complexity of triage and follow-up [Banovac, M. et al., 2017]. Risk minimisation studies demonstrate that risk minimisation plans are not enough; the effectiveness must be measured using credible measures and designs [Vora, P. et al., 2018]. Electronic surveillance research provides a warning: more sources may provide more information, but also more confusion, noise and the risk of adverse outcomes if the procedure lacks justification [Caster, O. et al., 2018].

Table 2 examines methods from the studies included; it reveals that different methods have yet to converge on a model of readiness. Database

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studies report evidence of reporting but may not report evidence of whether a company's procedures allow or disallow late reporting or poor quality reports. Systematic reviews make claims about interventions, but not generalisation of inspection evidence. Electronic studies applying computational and artificial intelligence identify signal opportunities, but the regulator will still be interested in validation, interpretability, change and human oversight. We also see a gap between the pharmacovigilance study evidence and the inspection evidence.

Table 2. Method comparison

Ref	Method	Strengths	Limitations
[Tobaiqy, M. et al., 2021]	Descriptive analysis of publicly accessible pharmacovigilance database content.	Provides direct insight into centralised reporting visibility, public data availability, and the role of database transparency in safety review.	Does not reveal company-level root causes behind incomplete reporting, delayed submission, or weak internal reconciliation.
[Vora, P. et al., 2018]	Review of registered studies evaluating risk minimisation measure effectiveness.	Connects regulatory risk controls to post-authorisation evidence generation and highlights endpoint choices relevant to inspection review.	Heterogeneous designs and incomplete implementation measures limit comparability across products and regulatory contexts.
[Goedecke, T. et al., 2018]	Systematic review of regulatory intervention impact methods.	Clarifies methodological problems in measuring whether safety communications or restrictions change behaviour or outcomes.	Causal attribution remains difficult when background prescribing trends or parallel interventions affect observed outcomes.
[Caster, O. et al., 2018]	Empirical broad-range statistical signal detection in social media data.	Tests digital surveillance utility at scale and provides direct evidence against simplistic assumptions about social media signal value.	High noise and low clinical completeness limit regulatory reliance without strong filtering and documentation controls.
[Trifirò, G. et al., 2018]	Conceptual review of healthcare databases and emerging evidence sources.	Establishes data fitness, governance, and interpretability as prerequisites for meaningful safety surveillance.	Offers limited operational detail on how inspection teams should evaluate readiness maturity in real-world data programs.
[Caster, O. et al., 2020]	Statistical analysis guidance for disproportionality in small datasets or subsets.	Provides practical safeguards against false-positive safety associations in sparse or exploratory analyses.	Does not address organisational escalation pathways, documentation quality, or post-signal governance controls.
[Bate, A., & Hobbiger, S. F. 2021]	Conceptual analysis of automation and artificial intelligence in medicines safety.	Identifies governance risks created by automation, including explainability and human accountability concerns.	Lacks direct empirical measurement of inspection outcomes linked to automated pharmacovigilance systems.
[van Stekelenborg, J. *et al.*, 2019]	Technical review of text and data mining methods for adverse reaction detection.	Maps extraction methods, language-processing challenges, and performance constraints relevant to digital case discovery.	Technical emphasis leaves quality-system questions, audit trails, and regulatory defensibility underdeveloped.

The examples in Table 3 also show that the most important outcomes for inspection are not necessarily the most technically important outcomes. Social media studies often assess detection effectiveness, but readiness includes social media governance and escalation. Patient

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reporting studies often measure content of information, but readiness requires harmonisation of the information with clinical and regulatory timelines. Risk minimisation studies often assess behaviour or outcome, but readiness also includes documentation of the rationale for design of the measure, monitoring of the implementation and escalation in the event of ineffective implementation. This is why FDA, EMA and MHRA lessons cannot be reduced to individual skills.

Table 3. Results comparison

Ref	System / Context	Metric / Basis of Comparison	Outcome
[Tobaiqy, M. et al., 2021]	Centralised European safety database environment.	Public accessibility, structured data availability, and relevance for research and public health review.	Supports inspection emphasis on accurate submissions, traceable coding, and consistency between company records and regulator-visible data.
[Banovac, M. et al., 2017]	Patient reporting within European pharmacovigilance.	Contribution of patient-originated reports to safety evidence and report character.	Demonstrates added experiential value while increasing the need for controlled triage, follow-up, and clinical interpretation.
[Vora, P. et al., 2018]	Risk minimisation measure evaluation studies.	Study design, endpoint selection, and evidence of effectiveness measurement.	Shows that effectiveness evidence is uneven, creating inspection risk when risk minimisation is documented but not evaluated robustly.
[Goedecke, T. et al., 2018]	Regulatory intervention evaluation literature.	Methods for assessing impact after safety-related regulatory action.	Identifies methodological fragmentation and weak attribution as barriers to defensible inspection evidence.
[Caster, O. et al., 2018]	Social media signal detection through WEB-RADR.	Statistical signal detection performance and practical signal utility.	Indicates limited routine value for broad social media detection, supporting selective and justified digital monitoring.
[Rolfes, L. et al., 2015]	Patient and healthcare professional report comparison.	Differences in reported information and clinical detail.	Shows complementary report profiles, requiring source-sensitive quality checks and follow-up strategies.
[Trifirò, G. et al., 2018]	Healthcare databases and emerging data sources.	Data fitness, interpretability, and movement from scale to actionable intelligence.	Supports inspection focus on governance of real-world data rather than reliance on volume alone.
[Caster, O. et al., 2020]	Disproportionality analysis in small datasets or subsets.	False-positive risk and statistical interpretation under sparse data conditions.	Reinforces the need for documented signal validation and cautious interpretation of subgroup findings.
[Bate, A., & Hobbiger, S. F. 2021]	Automation and artificial intelligence in safety surveillance.	Human oversight, transparency, and system accountability.	Indicates that automated readiness depends on explainability, validation, change control, and documented expert review.

Figure 2 maps the evidence base reviewed into a "colour-coded" trend view of focus in the selected literature. This figure is not a bibliometric representation of the whole field, but instead a visual classification of the references included in this review, which shows a shift of focus from core governance and reporting concerns to digital, real-world, and automation-related concerns. This aids discussion with a visual representation of the disparity between prolific method innovation and sparse direct assessment of inspection-readiness

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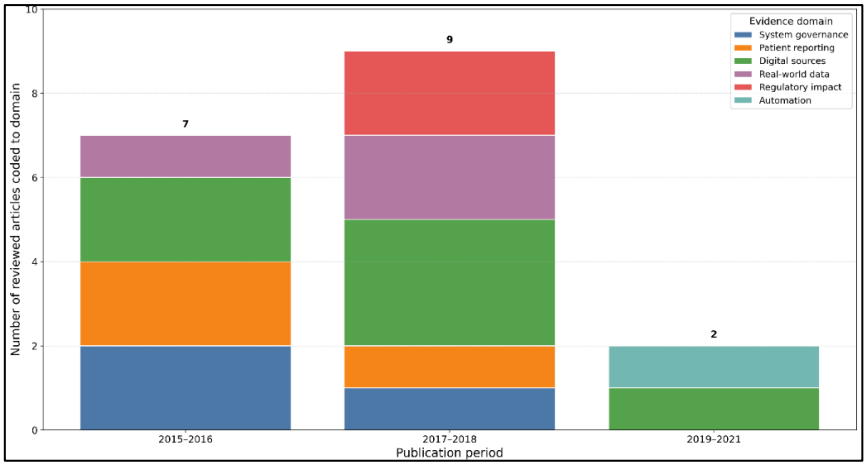


Figure 2. Thematic emphasis across reviewed inspection-readiness literature

Figure 2 suggests a strong focus on digital and real-world data in the literature, but automation later and inspection-specific governance less strongly. This is important because control as well as technology is the focus of FDA, EMA and MHRA inspections. The implication of a literature emphasis on new data, therefore, may not translate to readiness.

The regulatory takeaway is that FDA, EMA, and MHRA requirements converge on evidence control, although local implementation expectations differ. Readiness for FDA inspections is highly associated with rigour in post-marketing safety reporting, evidence from risk evaluation and mitigation strategies (REMS) (if applicable) and increased reliance on real-world data surveillance capability through Sentinel-based regulatory science *[Ball, R. et al., 2016; Platt, R. et al., 2018]*. EMA readiness has a strong focus on central system responsibility, EudraVigilance reporting and risk, signal and post-authorisation study management *[Borg, J. J. et al., 2015; Tobaiqy, M. et al., 2021]*. MHRA inspection readiness expectations are similar but with emphasis on United Kingdom-specific reporting, United Kingdom responsible persons, United Kingdom-specific signal processes and inspection readiness as a result of its exit from the European regulatory network. There are fewer peer-reviewed studies detailing empirical data of MHRA inspections, making it difficult for companies to compare readiness for FDA, EMA and MHRA.

To add a relational view of emphasis of FDA, EMA and MHRA inspection expectations, Figure 3 is offered. The bubble chart represents relative emphasis in a conceptual, review-based comparative, not scored, illustration. It illustrates the discussion by demonstrating emphasis on common controls and scope for jurisdictional differences in data management, risk management and local accountability.

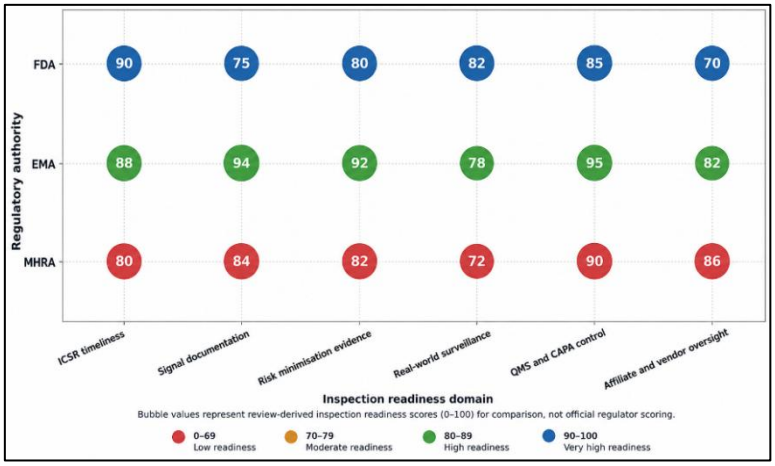


Figure 3. Comparative inspection-readiness emphasis across FDA, EMA, and MHRA domains

Figure 3's illustrates a key message for global pharmacovigilance: global harmonisation should not be at the expense of local details. A uniform process will help, but inspection readiness includes

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jurisdictional appendices, jurisdictional accountability registers and evidence that global processes are effective in the jurisdiction being inspected. The figure also shows why vendor and affiliate oversight is necessary because global safety data often flow through local or outsourced data sources to the central safety function.

The most obvious gap in the reviewed studies is the absence of evidence that readiness practices improve inspection outcomes. Studies exist that assess whether signals can be identified, whether patient reports are useful, whether electronic data can be used, and whether regulatory actions can be measured. But there is little peer-reviewed research on the effects of specific quality system practices on critical inspection findings, time to close CAPA, inspection classification and reducing deficiencies. This is because readiness for inspection is an outcome. Without performance-based readiness, companies might focus on "look-right" documentation and not focus on root cause analysis, control testing and CAPA effectiveness.

To assess readiness through the review, Figure 4 shows an application-specific risk map. The x-axis is the maturity needed to control the activity, and the y-axis is the likely consequence of the activity being deficient. The mapped areas show that some activities, such as signal governance and CAPA effectiveness, have high inspection consequence, despite not being technically complex.

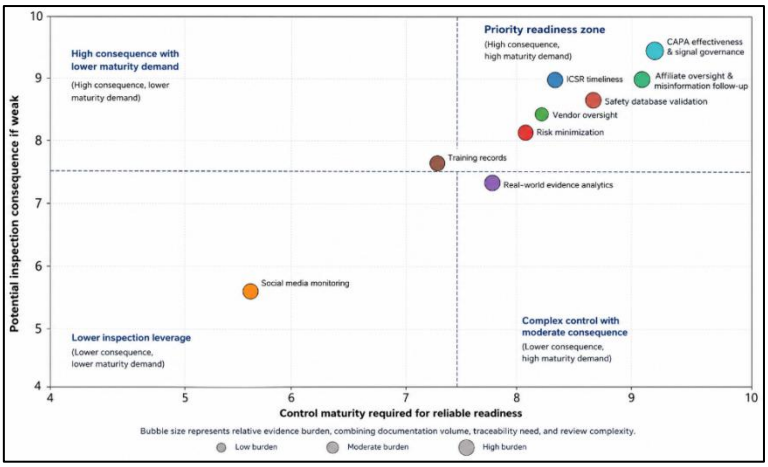


Figure 4. Risk-control map for pharmacovigilance inspection readiness domain

Figure 4 shows that process inventories are not sufficient to determine inspection readiness. Critical areas need regular testing of controls, trend monitoring and showing that corrective actions changed system behaviour. The map also implies that new domains such as social media monitoring are less important than signal governance and CAPA effectiveness unless a company has officially adopted such sources of data into regulated surveillance.

The literature also reveals a big data paradox. Big data are a growing part of pharmacovigilance, but inspectors will assess readiness in terms of complete, valid, accessible data that are connected to decision-making. Trifirò and colleagues' arguments for smart data, not big data, are relevant as data analytics without governance will be more difficult to defend than small data sets *[Trifirò, G. et al., 2018]*. Caster and colleagues' recommendations for disproportionality analyses on small data sets also make this point from a statistical point of view, as smaller analyses can yield more false positives unless we limit interpretation *[Caster, O. et al., 2020]*. So, for FDA, EMA and MHRA readiness, statistical expertise needs to be coupled with pre-determined thresholds, review minutes and escalation processes.

Automation exacerbates this issue. Machine learning can improve case ingestion, the identification of duplicates, literature search, narrative classification and prioritisation, but automation can also allow diffusion of accountability when model predictions are taken without review. Bate and Hobbiger's article is significant because it frames automation within a safety-system perspective *[Bate, A., & Hobbiger, S. F. 2021]*. Karimi and colleagues' survey of text mining approaches also shows that adverse event extraction is still prone to linguistically complex and ambiguous cases [Karimi, S. *et al*., 2015]. So, inspection readiness for automated pharmacovigilance requires model validation and monitoring, exception handling, versioning and proof that only safety experts make decisions.

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Another interpretation is the evidence distribution. EMA literature is strong due to robust literature on EudraVigilance, PRAC, post-authorisation studies and European risk minimisation evaluation. FDA-related literature is prominent in active surveillance and infrastructure (Sentinel). Literature on MHRA inspection expectations is important in practice, but less evident in recent articles that fit the article-only inclusion criteria. This is not to say that MHRA expectations are less important. Rather, it is a publications gap. Multinational companies should not misinterpret less published evidence as fewer inspections. And for readiness, it is prudent to assume that MHRA-specific expectations require regulatory intelligence, internal benchmarking and local evidence practices even if the peer-reviewed literature does not contain comparative studies.

FUTURE DIRECTIONS

The next frontier of inspection readiness research for global pharmacovigilance should shift the focus from component-level pharmacovigilance analyses to system-level empirical evaluation. The discipline needs research on patterns of inspection findings, recurring deficiencies, CAPA recurrence, vendor oversight, and readiness maturity and inspection outcomes. This would bridge the gap between the science of safety surveillance and FDA, EMA and MHRA regulatory inspections. Absent inspection-outcome studies, companies will need to continue translating indirect evidence into readiness programs via expert opinion rather than readiness models.

The second priority is comparative readiness measures that can be used across jurisdictions. FDA, EMA and MHRA expectations are similar but local emphasis varies on reporting pathways, responsible personnel, database interfaces and risk-management documentation. Future research could assess the capability of maturity scores to measure control performance in case management, signal management, risk mitigation, CAPA effectiveness, training, affiliate oversight, and vendor oversight. These should not be "checklist metrics". A robust maturity model will score quality of evidence, exception management, trend analysis, root-cause analysis and evidence of improvement.

A third area is electronic pharmacovigilance and automation. Studies should not only evaluate whether artificial intelligence, text mining, or automation enhances the detection of signals, but also whether systems remain inspection-ready under validation, change control, audit trail, human oversight, and human error recovery. Research should test manual, semi-automated and automated processes against metrics relevant to inspectors, such as traceability, reproducibility, false-negative control, escalation records and recovery from errors. This direction is achievable because automation is already entering pharmacovigilance practice, but the published evidence is stronger in technical rather than regulated operational control.

The fourth direction concerns patient reports, social media, and other novel sources. Published research indicates these sources are valuable, but noisy and variable in quality. Future studies should explore the effects of source-specific controls on case quality, seriousness, duplicate case identification and signal prioritisation. Inspection readiness would benefit from studies on criteria for when to monitor a source, how to enter information into the safety database, and how to document limitations. These studies would help determine what is meaningful source governance rather than excessive collection of low-value data.

Finally, global inspection readiness is an interdisciplinary effort between pharmacovigilance scientists, quality professionals, pharmacoepidemiologists, regulatory lawyers, data scientists, auditors, and organisational governance specialists. Accordingly, readiness should be a socio-technical system. Future research should investigate interactions between procedures, systems, skills, vendor agreements, data standards, analyses, and management. This would bring the literature more in line with FDA, EMA and MHRA expectations because inspections focus on systems, not individual methods.

CONCLUSION

Inspection readiness in global pharmacovigilance is best understood as a process of continuous evidence generation that connects safety data collection, scientific assessment, regulatory reporting, and quality-improvement activities. The literature reviewed for this article demonstrates that current pharmacovigilance encompasses more than spontaneous reporting, but expansion is not synonymous with readiness. Readiness is achieved when expanded evidence sources are controlled by validated systems, procedures, judgement and corrective action.

The key takeaway message from FDA, EMA and MHRA expectations is that regulatory harmonisation occurs at the level of control

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architecture, even if local regulations vary. Timely reporting, signal documentation, risk minimisation evidence, quality-system oversight and traceable decision-making processes are at the heart of all three systems. A truly global system of pharmacovigilance must therefore maintain a uniform control framework while documenting local evidence for local inspection evaluation.

The literature also reveals persistent gaps. There remains little direct peer-reviewed evidence on inspection findings, inspection outcome predictors, readiness maturity, and so on. Numerous research papers focus on tools, sources of data, or data analysis, without testing whether tools enhance compliance. This leaves a future need for linking pharmacovigilance science with inspectable organisational control.

Inspection readiness in the future will rely on prudent integration of digital solutions, real-world evidence, patient reporting and automation into quality systems with accountability. Innovation will only enhance pharmacovigilance if it is transparent, validated, proportionate and guided by competent safety leadership. Therefore, the discipline needs to move beyond inspection readiness to continuous regulatory readiness.

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