DCVMN Pharmacovigilance Training
Workshop 13 May 2021

dcvmn
Developing Countries Vaccine Manufacturers Network

Critical pharmacovigilance processes and business continuity

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Setting the Scene

I.B.11.3. Critical pharmacovigilance processes and business continuity

Critical Processes /1
GVP Module 1

Case processing	• Collection, processing, management, quality control, F/U for missing info, coding, classification, duplicate detection, evaluation and timely (electronic) transmission of ICSRs from any source • Interaction between PV and product quality defect systems
Ongoing safety evaluation / Signal management	• Continuous safety profile monitoring and benefit-risk evaluation • Signal management • Scheduling, preparation, submission and assessment of PSURs • Keeping product information up-to-date with current scientific knowledge, incl. conclusion of assessments and recommendations of the NRA
Risk Management System and Risk Minimization Commitments	• Establishing, assessing and implementing risk management systems and evaluation of risk minimization effectiveness • Meeting commitments and responding to request from NRAs, incl provision of correct and complete information

Critical Processes /2
GVP Module 1

Communication	• Communication about safety concerns between MAHs and NRA, in particular notifying changes to the B/R balance • Communication of information about changes to the B/R balance to patients and HCP for safe and effective use
Third party obligations	• Identification of licensing partners • Adequacy of existing pharmacovigilance agreements • Procedures covering new licensing arrangements
Registration activities Regulatory intelligence	• Implementation of MA variations for safety reasons according to urgency required • Awareness of applications for marketing authorization • Awareness of changes to regulation
Safety database and associated systems	

Critical Processes - Common Inspection findings

- Failure to submit or late expedited and periodic reports
- Inaccurate or incomplete reports to Authority questions or requests
- Failure to do follow-up for serious and unexpected AEFIs
- Lack of or inadequately written SOPs
- Failure to follow the company's own SOPs
- Database issues, incl. inadequate validation and security
- Deficiencies of QPPV (if applicable)
- Technical issues: incorrectly formatted submissions and reports
- Poor quality of PSURs or ICSRs Common Inspection findings
- Safety signals missed, ignored, or poorly assessed
- No or poor-quality risk management processes
- No or poor-quality pharmacovigilance management system
- Labeling problems (e.g., CCSI, SPC, package insert, patient information)
- Lack or inadequate metrics and performance measures
- Problems and CAPAs not corrected / done and / or promises not kept

Business continuity

GVP – Module 1 - Risk-based approach

Organization	• Provisions for events that could severely impact the organization / staff
Infrastructure	• Provisions for events that could severely impact infrastructure in general or PV structures and processes in particular
Back-up Systems	• Systems for urgent exchange of information within organization / amongst organizations sharing PV tasks, and between MAH and NRAs

Business Continuity and Disaster Recovery

Business Continuity: Capability of the MAH to continue the critical PV processes at a pre-defined acceptable level following a disruptive incident

Business Continuity Planning (resiliency planning): Process of creating a system of prevention and to document the outlines how the PV system will continue to operate during an unplanned disruption

Disaster recovery: Policies, tools and procedures to enable the recovery or continuation of vital infrastructure and systems following a natural / human-induces disaster.

- Focus mainly on IT systems and technology systems supporting critical processes / functions

Business Continuity Plan (SOP)

Purpose

- Overview of the Business Continuity System

Crisis Management and Business Continuity Structure

Pharmacovigilance Business Continuity Plan (BCP)

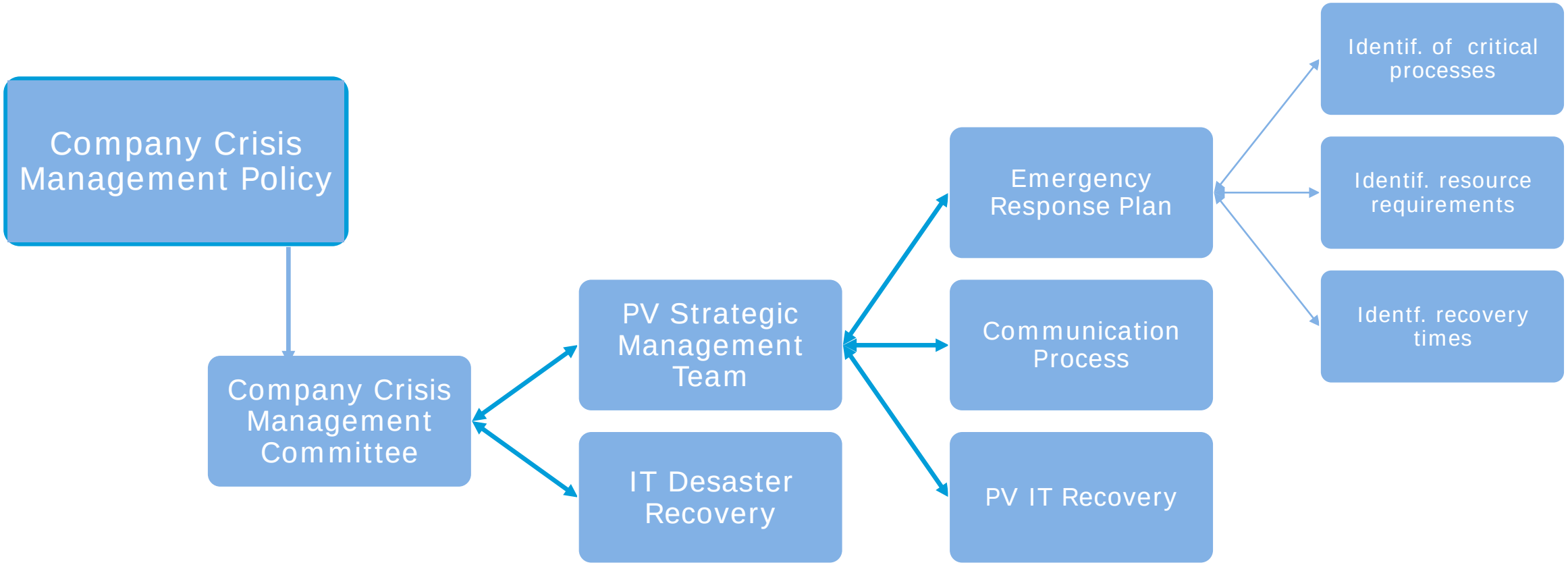
- Critical processes
- Content of a BCP
- BCP activation

Notification and Communications

Roles and responsibilities

Pharmacovigilance Process Recovery Strategies

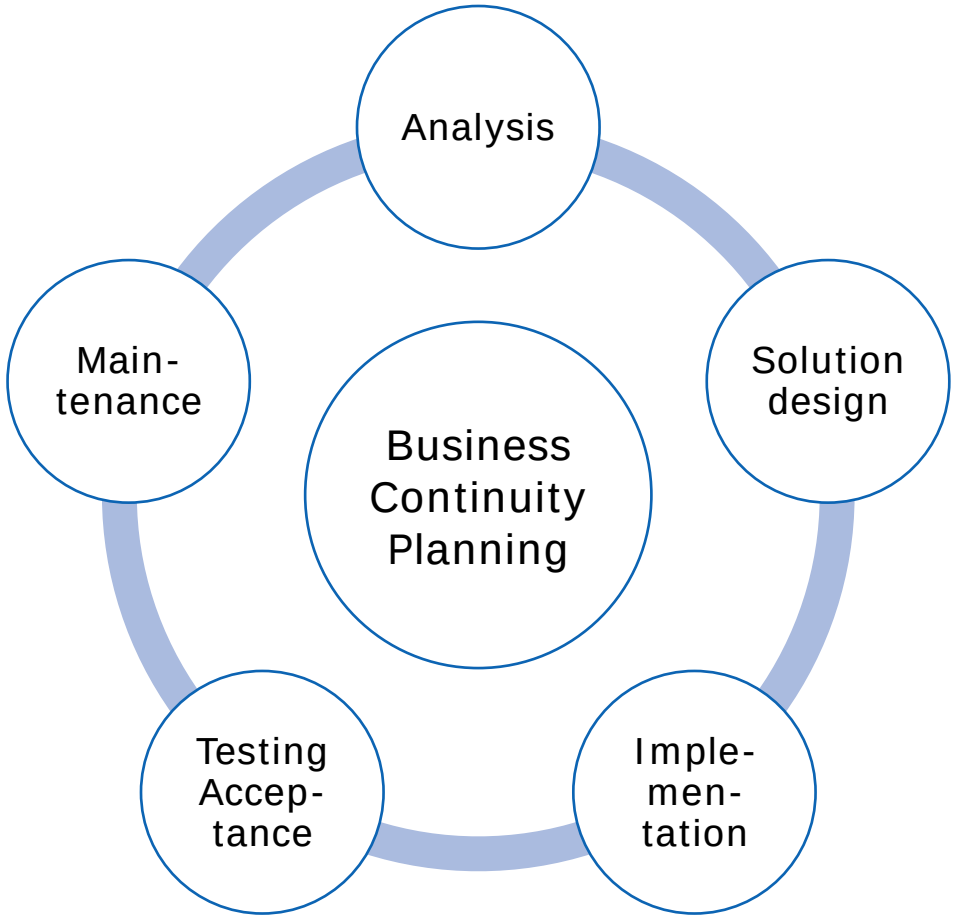
Company Crisis Management and Business Continuity Structure - Example



Content of Business Continuity Plan

- Describe activation criteria and procedures
- Structure, roles, authorities, responsibilities to implement temporary solutions
- Response and recovery actions for critical business processes, incl. workarounds for eg staff shortages, loss of IT applications etc.
- Any related functional area identified for BCP responses
- Communication process and contact details for staff and other stakeholders.
- Internal and external interdependencies and their business continuity plans
- Resource requirements, especially alternate work areas for key staff if required.
- Information flow and documentation processes.
- How to cope with the temporary or permanent loss of key personnel.

Business Continuity Planning Lifecycle



- Inventory:
  - Equipment
  - Locations/ officies/ work area
  - Documents and documentation (incl. Off-site back-ups)

- Business Impact Analysis
  - Human resources
  - IT systems
  - Physical assets (mobile phone, laptops / workstations)
  - Documents and documentation (electronic and physical)
  - Recovery Point Objective (acceptable latency of data not recovered)
  - Recovery Time Objective (acceptable time to restore function)

PV Process Recovery Strategies - Example

Critical Processes Desaster scenarios	RTO	Workarounds	People required at RTO	Equipment required at RTO
Reporting of serious AEFIs / SAE	24 h	……..	…….	Laptops, mobile phones
Communication of critical safety infomation	immediate	…….	……	Laptops, mobile phones
……				
…..				
….				

Inspection topics

Topic Area	Sub-topic of reported findings
Collection and collation of adverse reactions	• Spontaneous sources of safety data, e.g., medical information, product quality complaints • Literature searching • Solicited sources of safety data
Management of adverse reactions	• Case processing: data entry, coding, assessment, follow-up and reporting • Data management, including migration of safety data
Risk management	• Management of additional PV activities as part of RMP • Maintenance of reference safety information • Additional risk minimization activities as part of RMP • Safety communication • RMP maintenance
Quality management system	• Procedures, record management, training, PV contracts • Audit and deviation management, incl. CAPA management • PV system oversight and governance, incl. Performance monitoring and role of QPPV • Information technology systems and applications
Provision of infpormation for supervisiion by national authority and inspection	• Inspection readiness • Management of the description of the pharmacovigilance system • Submission of information to national authorities
Clinical trials pharmacovigilance	• Clinical trials pharmacovigilance (e.g., maintenance of RSI for clinical trials, SUSAR reporting

Inspection Findings

Example: Critical Findings from MHRA PV Inspections 2018

Risk management systems
Significant deficiencies were identified across the risk management system for products reviewed during the inspection.

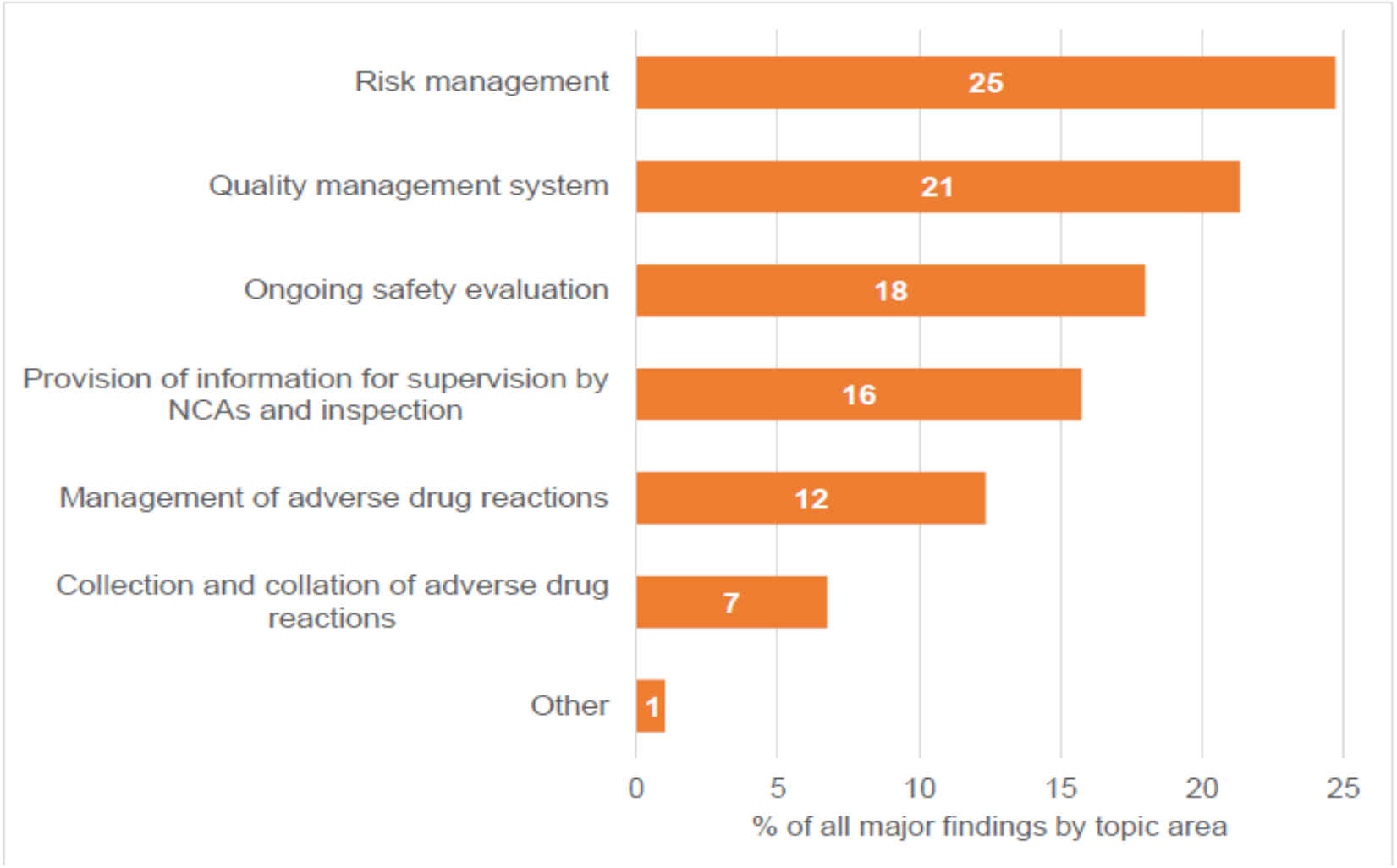
Additional risk minimisation measures, provision of information to national competent authorities and management of non-compliance
There were failures in the implementation of an electronic risk management system linked to a condition of specific marketing authorisations. These failures meant that reports submitted to the MHRA on the effectiveness of and adherence to additional risk minimisation measures were inaccurate.

Quality management system for pharmacovigilance
The inspection reported widespread failures in the delivery of pharmacovigilance across critical pharmacovigilance processes. Specific critical processes that were not being fulfilled according to the legislative requirements included risk minimisation, submission and preparation of PSURs, submission of ICSRs and the maintenance of product information.

Ongoing safety evaluation – Signal management
The MAH did not have the appropriate mechanisms and systems in place to allow for adequate ongoing safety monitoring, including signal detection.

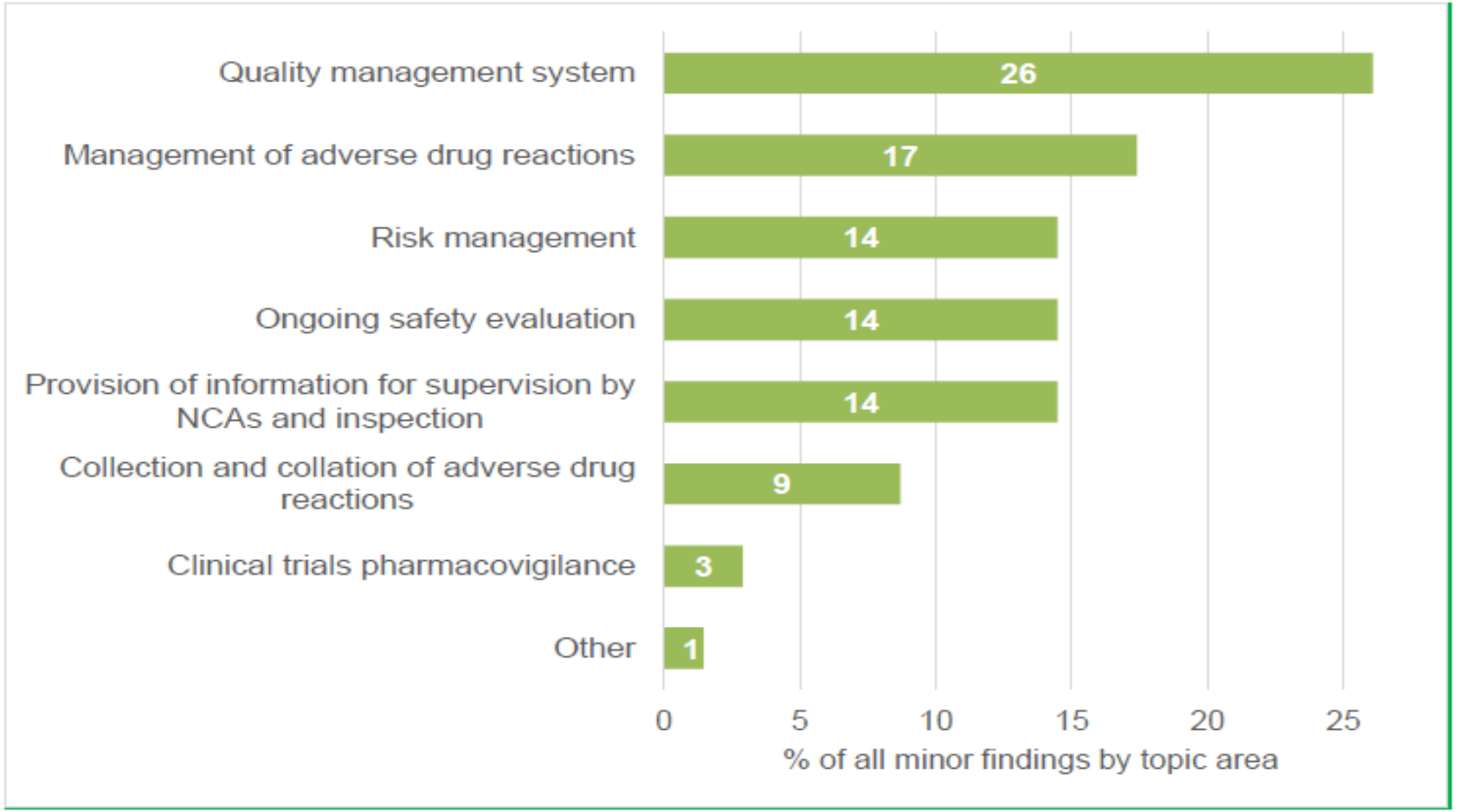
Inspection Findings

Example: Major Findings from MHRA PV Inspections 2018

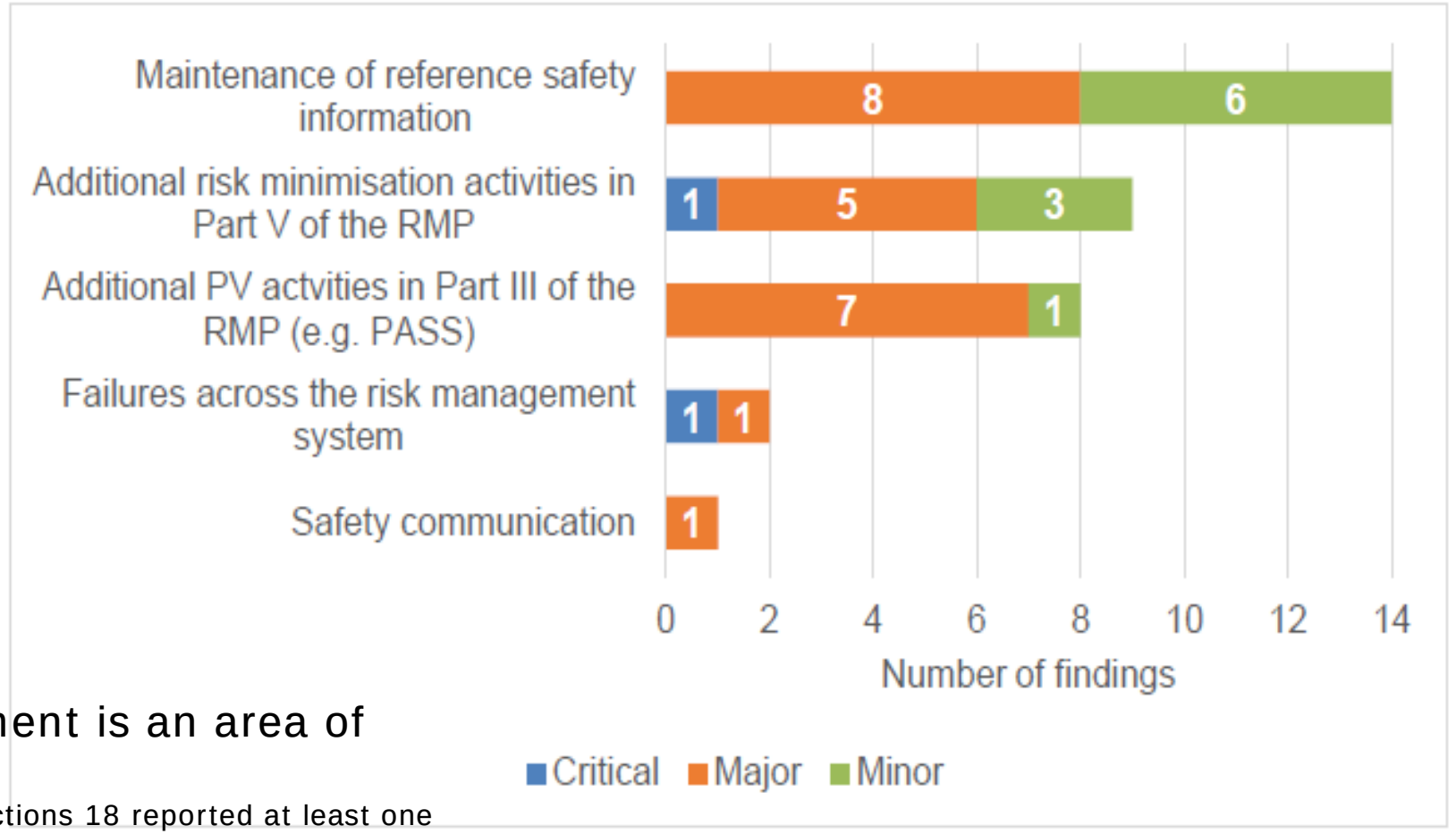


Inspection Findings

Example: Minor Findings from MHRA PV Inspections 2018



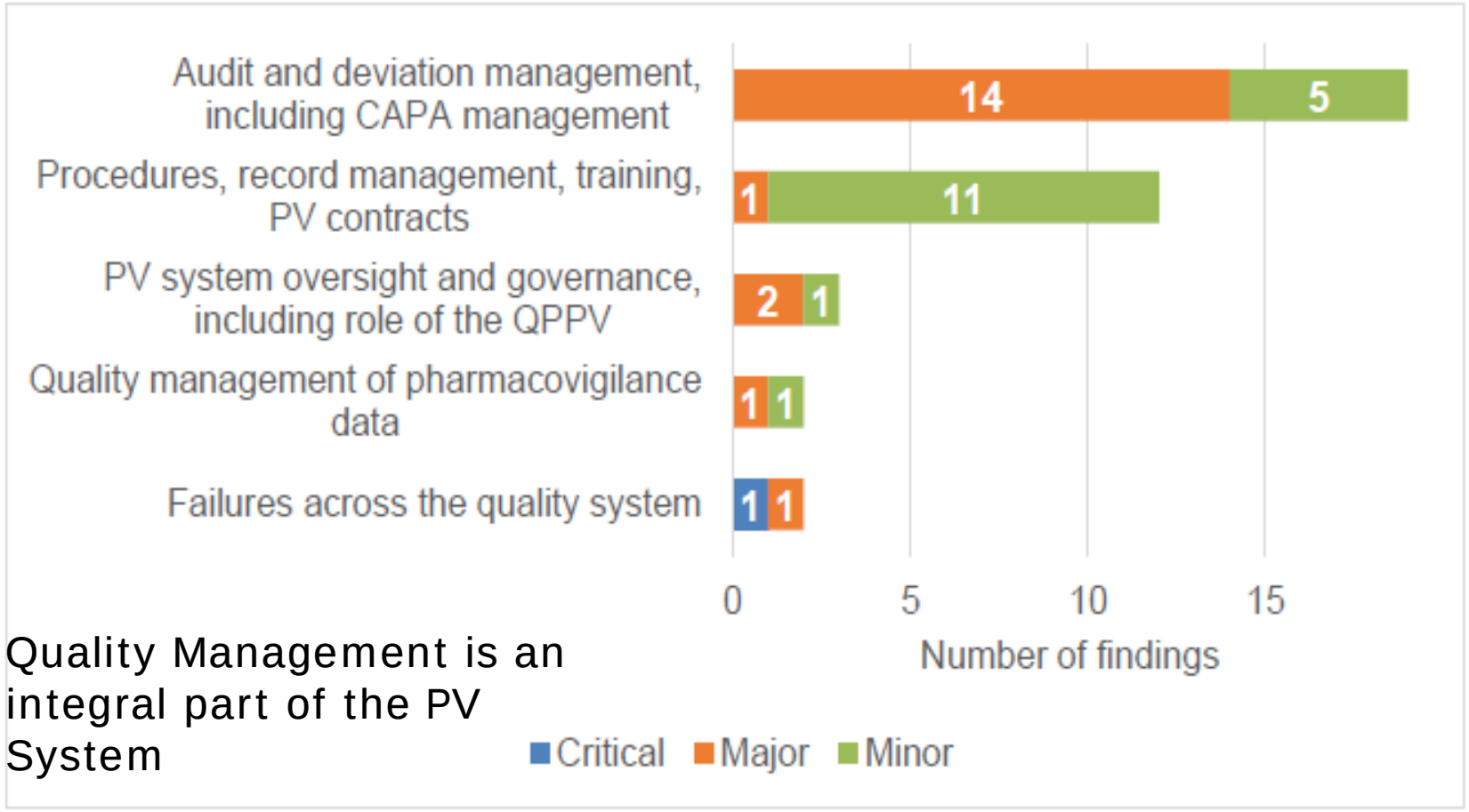
Inspection Findings
Example: Focus topic Risk Management



Risk Management is an area of concern

From 22 inspections 18 reported at least one finding of any grading

Inspection Findings
Example: Focus topic Quality Management



Quality Management is an integral part of the PV System

Representative Findings from Case Study

High-level Category	Sub-Category	Criticality	Observation	Regulatory Reference
Global				
Quality Control		Critical	The Department does not produce basic metrics easily or accurately (See Appendix I for additional comments on this issue). Drug Safety Operations took several days and several versions to produce basic metrics. It was impossible to ascertain how many cases the two safety systems contain and two searches yielded very different results. Compliance metrics produced by the CRO are not taken from the safety system (they are taken from the Access tracking database) so there is the potential for the CRO and the Company to produce different metrics.	EMEA CPMP/PhVWP Section 4.1
Data Quality		Important	In the two CRO locations, SAEs in the narrative are not coded.	MedDRA MSSO Points to Consider Document
IT		Important	In the US, users indicated that the safety system did not meet their requirements (e.g., reporting requirements). These issues would likely have been caught if users from all sites had been involved in defining and testing system requirements	Best Practice

Examples from SJ Pharma

Representative Findings from Case Study (Cont.)

High-level Category	Sub-Category	Criticality	Observation	Regulatory Reference
Japan				
Safety Process / Japan	Quality Control	Critical	Drug Safety Operations does not routinely monitor its compliance figures and cannot therefore implement measures to continuously improve it.	ICH GCP Section 5.1.1 EMEA CPMP/PhVWP Section 4.4
	Risk Management	Critical	There are essentially no risk management activities as such. There is a continuous analysis of certain side effects that are already known but no activities on signal detection, development of pharmacovigilance plans or risk minimization action plans.	FDA Guidance on Risk Management, March 2005 ICH E2E, Pharmacovigilance Planning
	SOP	Critical	Lack of standard business practices locally, in particular with handling of literature cases. For example, literature citations (author, journal, date, etc.) are not entered into the safety system. In general, staff interviewed could not demonstrate consistency in the performance of given tasks. There are no SOPs for the IT organization, and ARISg SOPs are in English only.	EC's Detailed guidance on the collection…* Section 6.1 EMEA CPMP/PhVWP Section 4.1 EMEA Volume 9, Section 1.1.1 ICH GCP Section 5.1.1

Examples from SJ Pharma

THANK YOU

Questions ?