DCVMN Pharmacovigilance Training
Workshop 5
14 July 2021

dcvmn
Developing Countries Vaccine Manufacturers Network

ICSR* / AEFI Receipt, Handling, Follow-up and Reconciliation

*ICSR: Individual Case Safety Report

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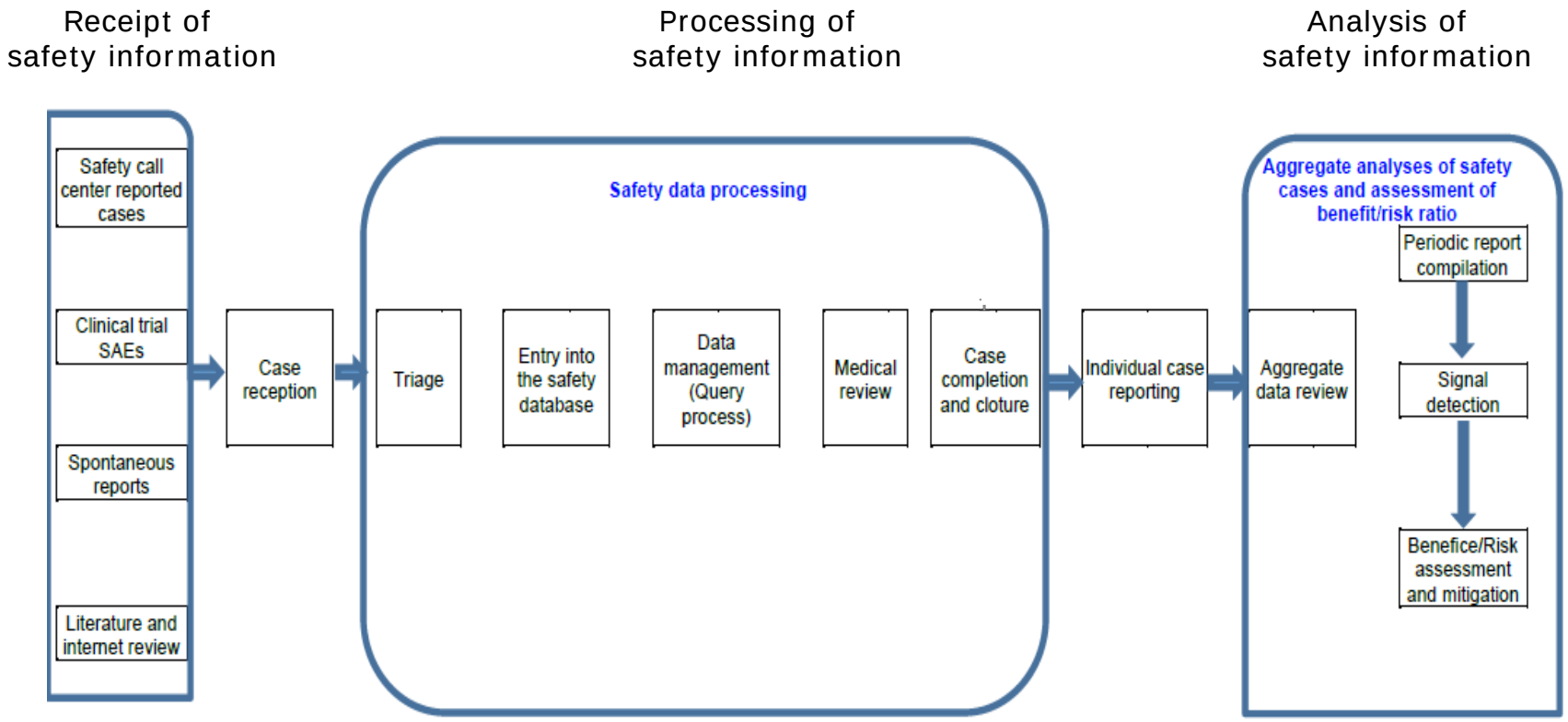
Pharmacovigilance activities Workflow



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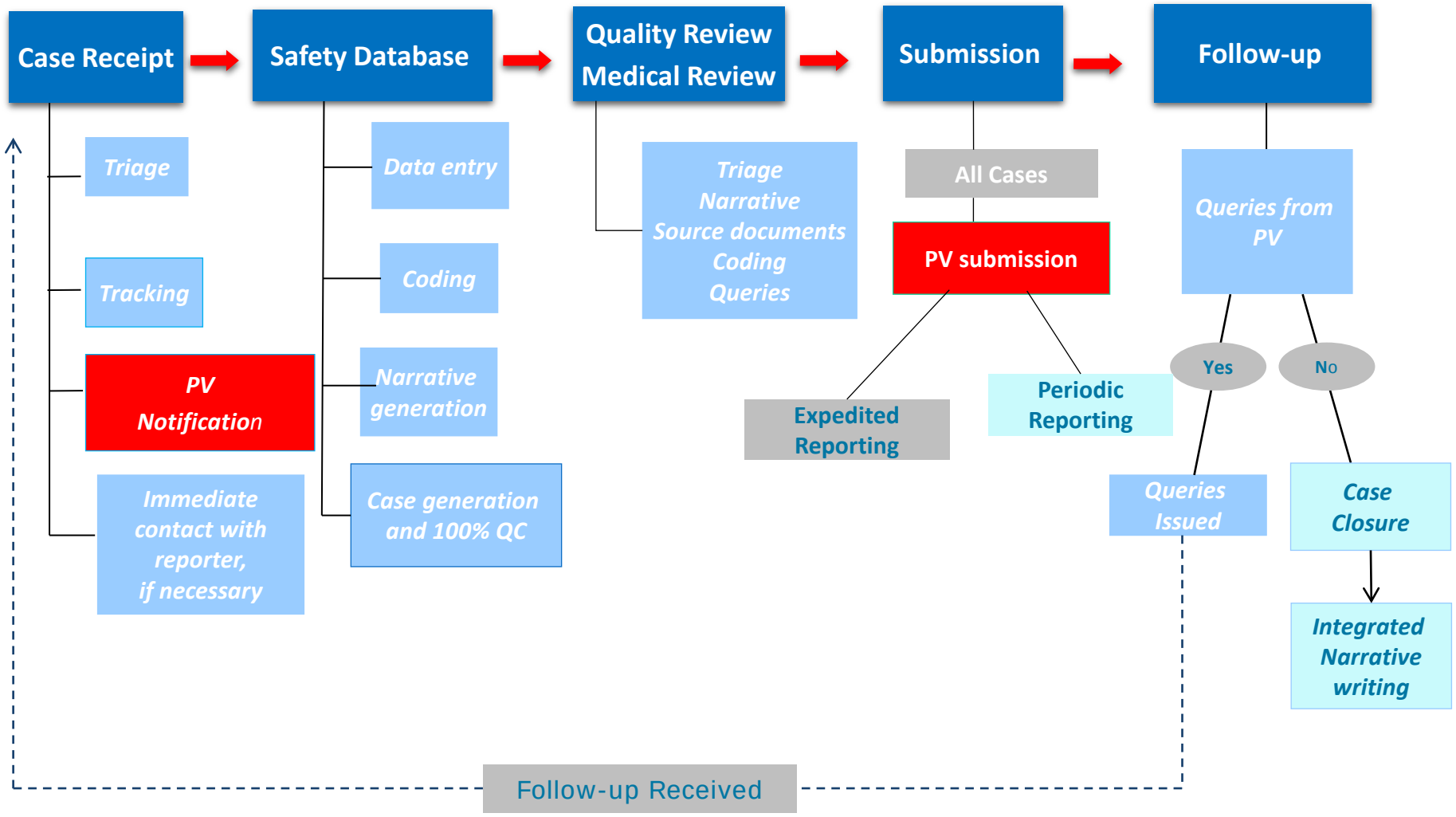
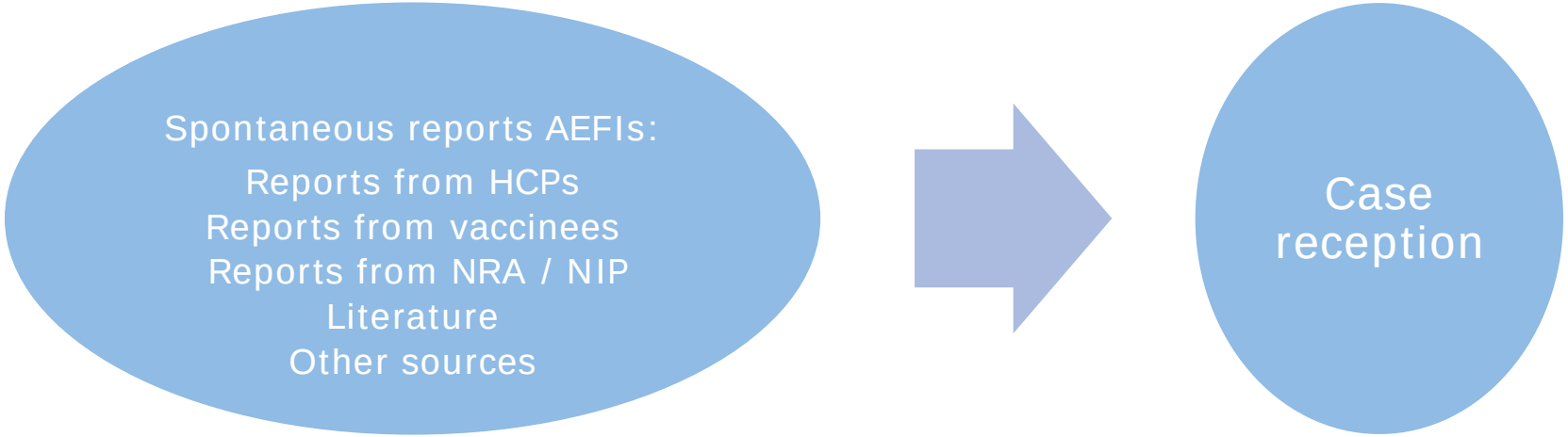
Safety data processing
AEFI case handling workflow



Case Receipt

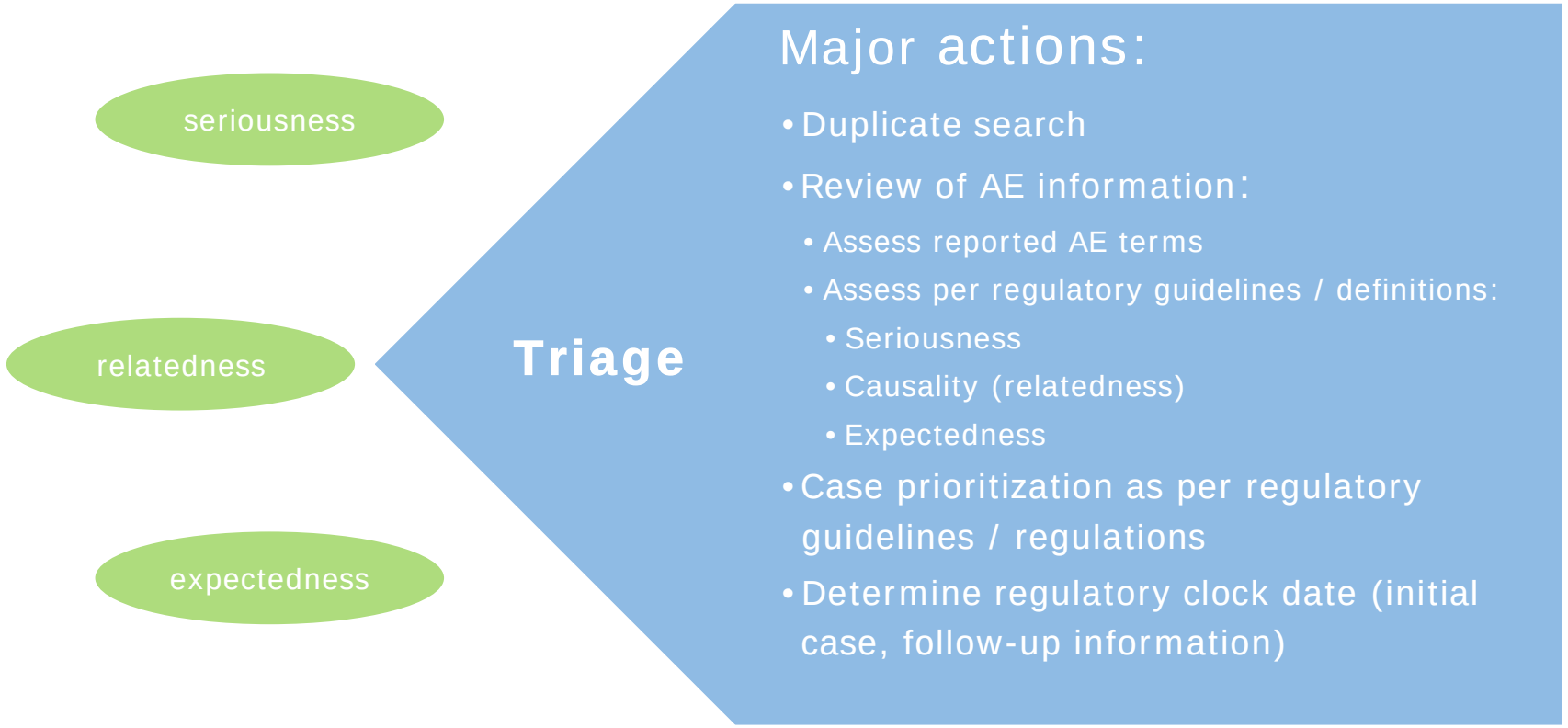


Major actions:

- Case intake / date of receipt (clock date)
- Acknowledge receipt
- Assign case number *
- Tracking of case receipt
- First check of case validity
- Request additional information, where necessary
- Translate AEFI into English, if appropriate

* depending on the PV database system (manual or electronic)

Case Triage


seriousness
relatedness
expectedness
Triage
Major actions:
• Duplicate search
• Review of AE information:
• Assess reported AE terms
• Assess per regulatory guidelines / definitions:
• Seriousness
• Causality (relatedness)
• Expectedness
• Case prioritization as per regulatory guidelines / regulations
• Determine regulatory clock date (initial case, follow-up information)

Seriousness assessment

- Assessment based on **outcome** of the AEFI
- ICH E2A seriousness criteria:
  - results in death
  - is life threatening
  - requires hospitalization or prolongation of hospitalization
  - results in persistent or significant disability
  - is a congenital anomaly
  - is medically important

Requires medical judgement

Requires medical judgement

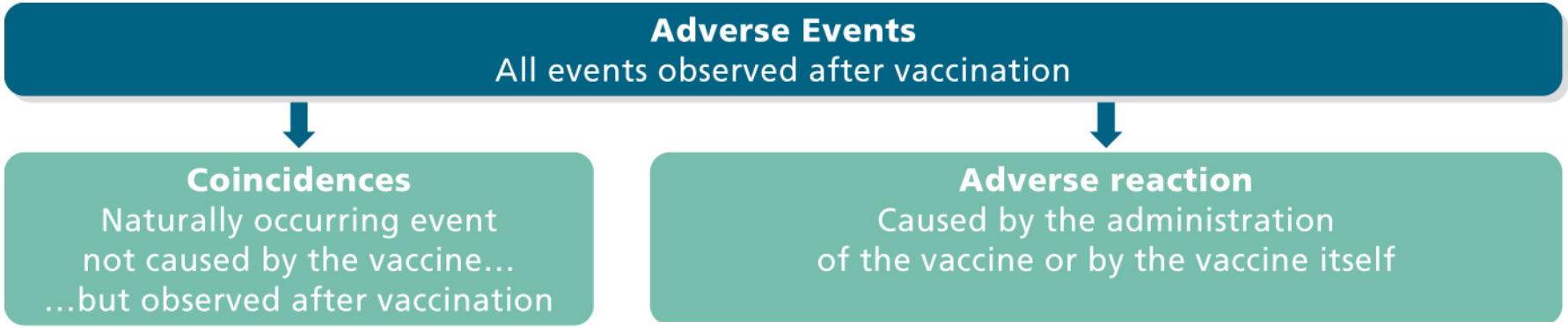
Requires medical judgement

Determines expedited regulatory reporting of AEFI

Specificities of seriousness assessment

- Death: only serious if event caused death
- Hospitalization: only serious if inpatient stay (e.g., overnight), not emergency room
- Life-threatening / medically important (i.e., serious in the medical sense): requires individual medical assessment
- Company (MAH): Adverse Events of Special Interest (AESI) / designated AEFIs (MedDRA coded)
- CIOMS V / WHO Critical Term List (MedDRA coded)
- EU: Important Medical Event (IME) List (MedDRA coded)

Relatedness (Causality)
Adverse Events following immunization AEFI



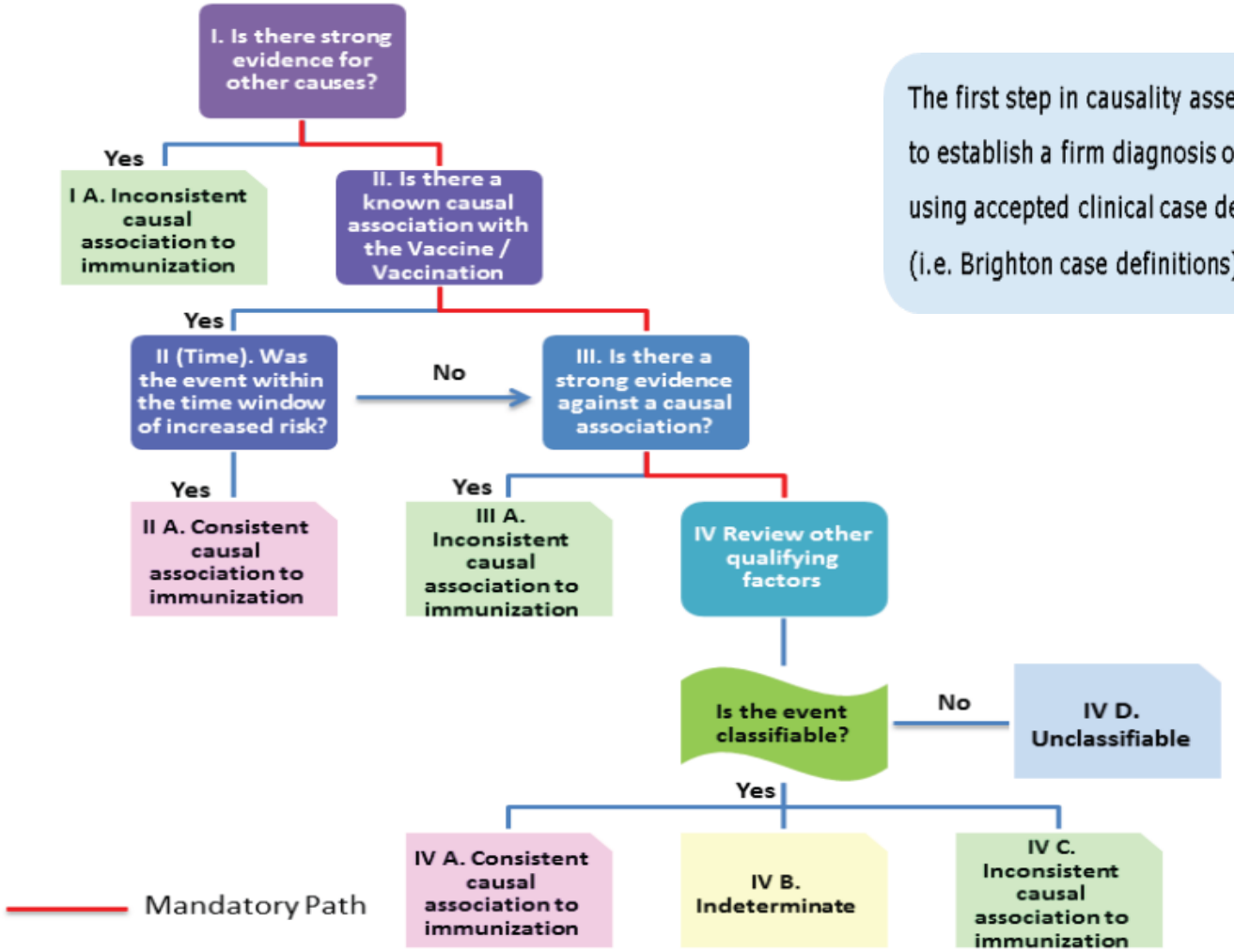
- Vaccine product related reaction
- Vaccine quality defect related reaction
- Immunization error related reaction
- Immunization anxiety related reaction

AEFI (WHO/CIOMS): Adverse medical occurrence following immunization and which does not necessarily have a causal relationship with the usage of the vaccine (**ICH E2A)**

Components of causality assessment

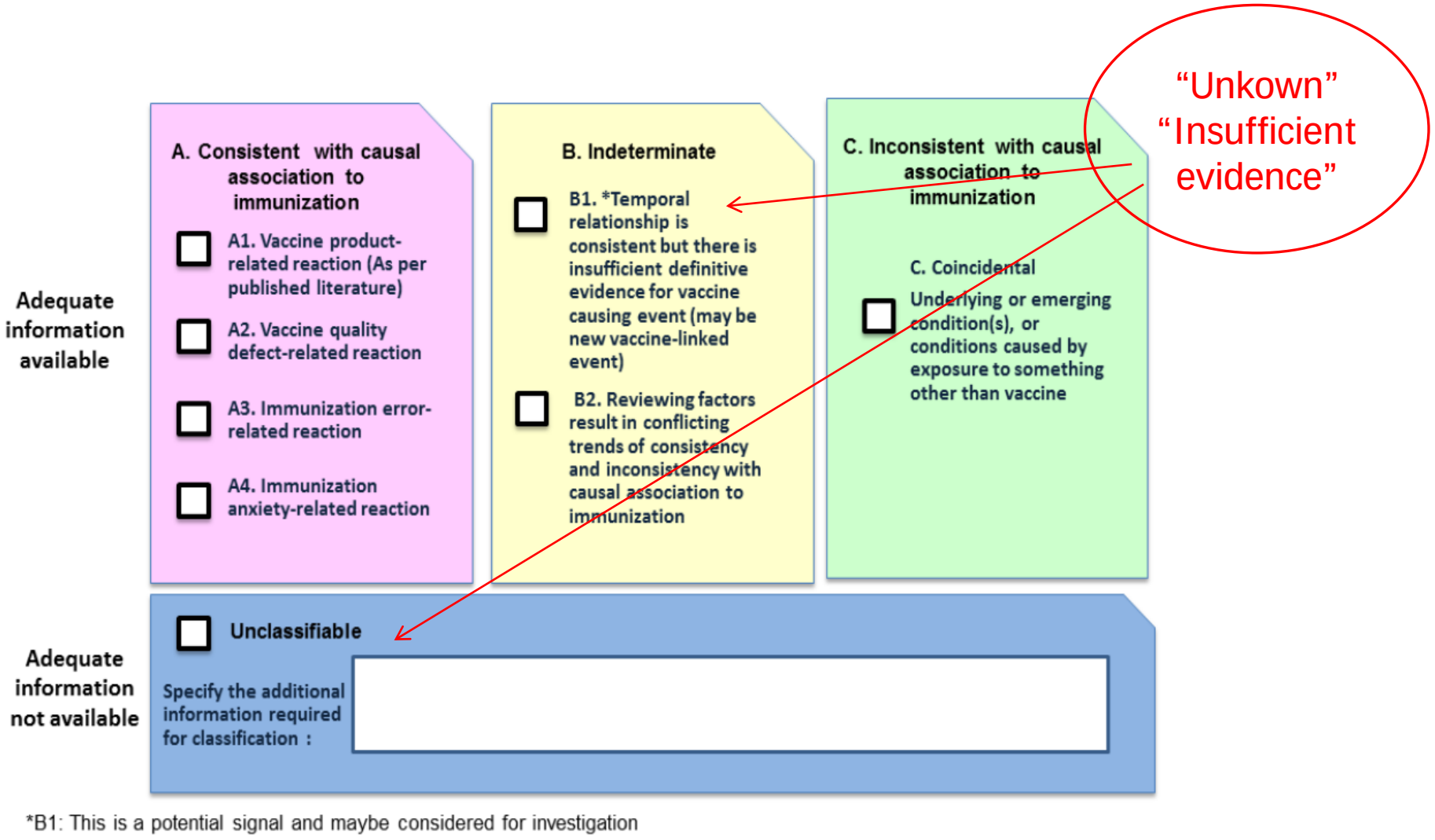
Eligibility	Determine if information collected in AEFI case investigation is sufficient for conducting causality assessment (e.g, Brighton case definition available?)
Data review	Review of specific and essential information to assess causality (e.g., good case quality)
Algorithm	Guide in the interpretation of available data and review their consistency
Classification	Classify the AEFI in one of the four final WHO categories to facilitate appropriate actions (unclassifiable, consistent, indeterminate, inconsistent)

Causality Assessment
WHO Algorithm



The first step in causality assessment is to establish a firm diagnosis of the AEFI using accepted clinical case definitions (i.e. Brighton case definitions)

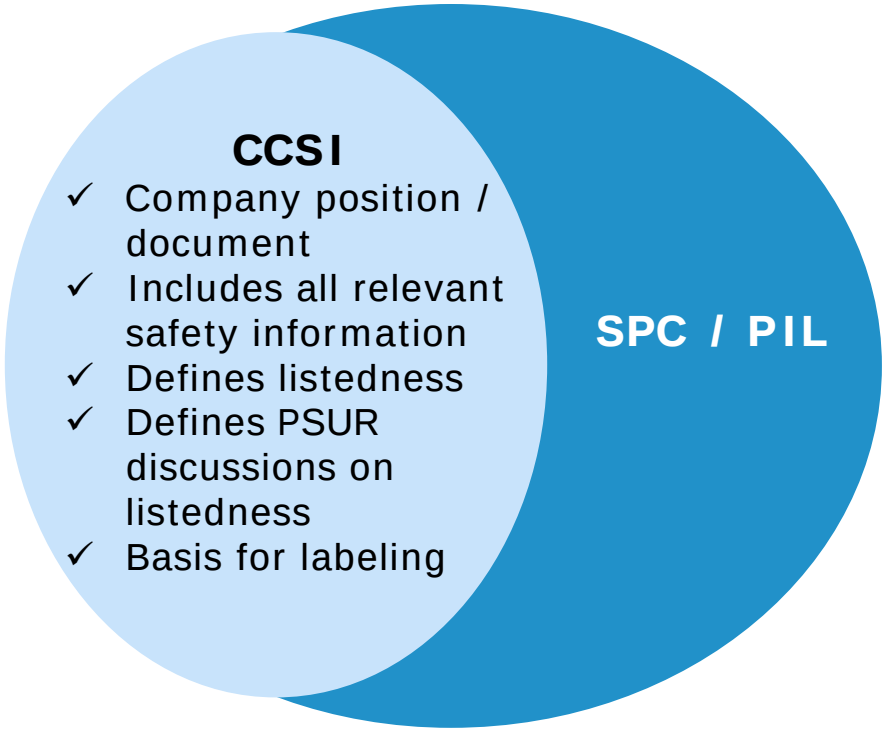
WHO Guideline on Causality Assessment



*B1: This is a potential signal and maybe considered for investigation

Expectedness in regulatory reporting

Expectedness of an AEFI depends on the Relevant Safety Information (RSI)
ICH E2A / ICHE2D

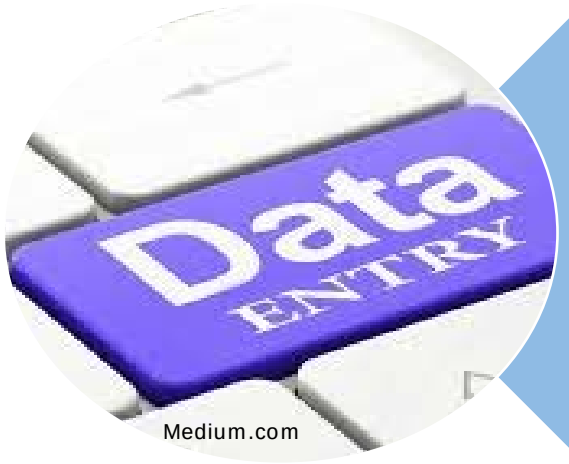


SPC - Summary of Product Characteristics
PIL - Patient Information Leaflet:

- ✓ Medico-legal document
- ✓ Safety information approved by Regulatory Authority for health professionals and patients
- ✓ Defines expectedness
- ✓ Basis for expedited regulatory reporting

CCSI: Company Core Safety Information

Data entry



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Major actions:

- Assign case identification number*
- Perform data entry
- Medical Coding:
  - AEFI terms
  - Medical history
  - Vaccine
- Generate narrative
- Analysis of similar events

* depending on the PV database system (manual or electronic)

Medical Coding

MedDRA® -Medical Dictionary for Regulatory Activities

Medical dictionary for all activities in the frame of Regulatory Activities

- The terminology is used through the entire regulatory process, from pre-marketing to post-marketing, and for data entry, retrieval, evaluation, and presentation
  - To standardize the communication during the whole life-cycle of a product
- Supports electronic reporting of ICSRs and eCTD
- Annual updates (version 24.0 March 2021)

Requires license

Price depends on the annual revenue of the company

Fee waiver for SMEs using EVWEB to fulfill reporting obligations in the EU

Quality review

Major actions:

- Quality review (QC) 100%
- Check case for accuracy
- Check case for completeness
- Check case for consistency
- Ensure correct coding (AEFI, medical history and product
- Check seriousness and labeling (expectedness)

Medical review

Major actions:

- Confirm triage (prioritization)
- Check case for medical sense
- Check and confirm medical coding
- Check and confirm seriousness and labeling (expectedness)
- Make company causality assessment from medical point of view and / or upgrade reporter causality
- Request non-routine follow-up, if appropriate
- Review the data for potential signals

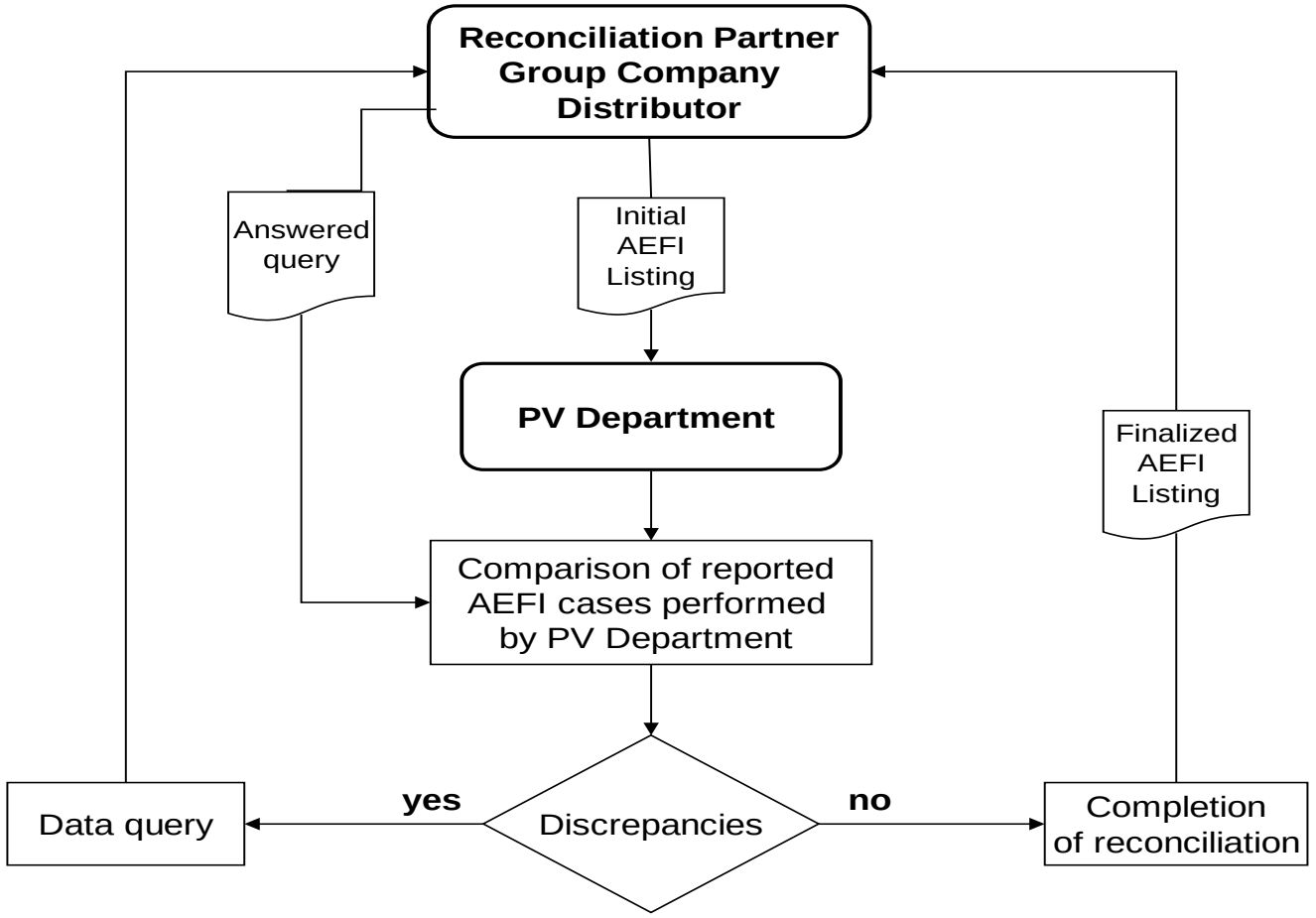
There is no actual regulation (FDA, EMA, MHRA) that requires a physician to review ICSRs, however medically qualified personnel should review all cases.

Distribution of ICSR Reconciliation

Major actions:

- Submission of expedited report (e.g., 15 day report) according to regulatory requirements (i.e., national / global)
- Distribution to business partner as per Safety Data Exchange Agreement (SDEA)
- Distribution to Safety Monitoring Committee (SMC), if applicable
- Confirm receipt of acknowledgement
- Reconciliation with external data collection partners
- Reconciliation with product quality complaints and medical information queries

Reconciliation

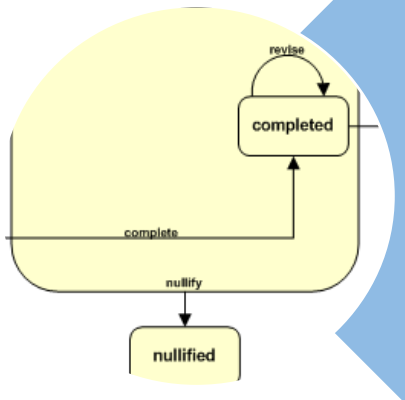


Parameter/variable	Requirement
PV Manufacturing Company Number (MCN)	exact match, if applicable
Other Reference No.	exact match
Product name	exact match
Country of report	exact match
Primary source	exact match
Patient information	exact match
Type of report	exact match
Receipt date	exact match
Batch No.	exact match
Reported term	plausible/consistent

Example of AEFI listing for reconciliation

Internal Reference Number	Country	Patient age	Patient sex	Product Name	Batch number	Reported Term	Date received	Initial/ Follow-up/ Duplicate	Date sent to PV

Case completion - Case closure (locking)

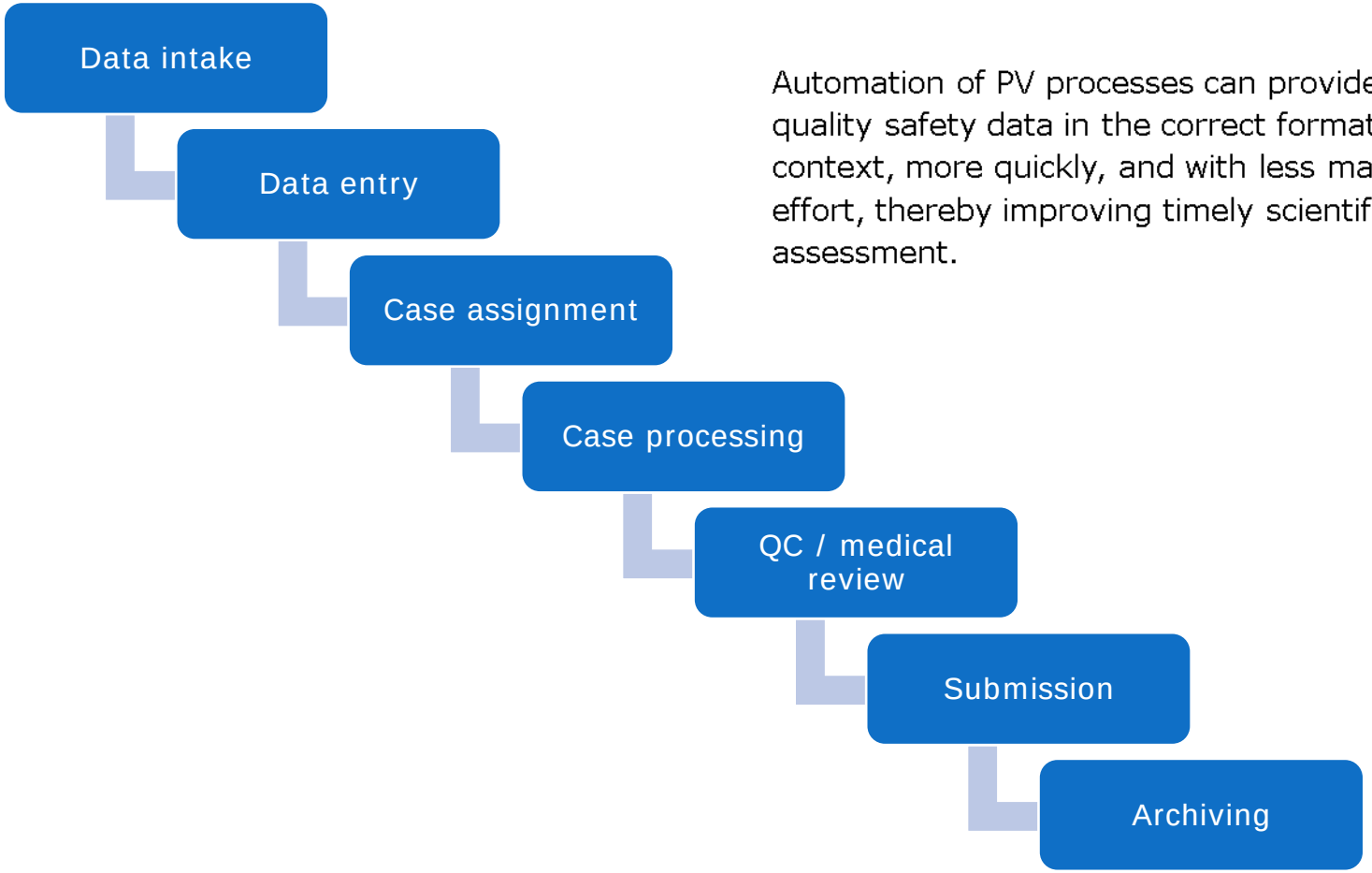


Major actions:

- Ensure all data are corrected
- Incorporate any request changes
- Ensure that all follow-up action are completed
- Ensure that no changes can be made after locking in the case*

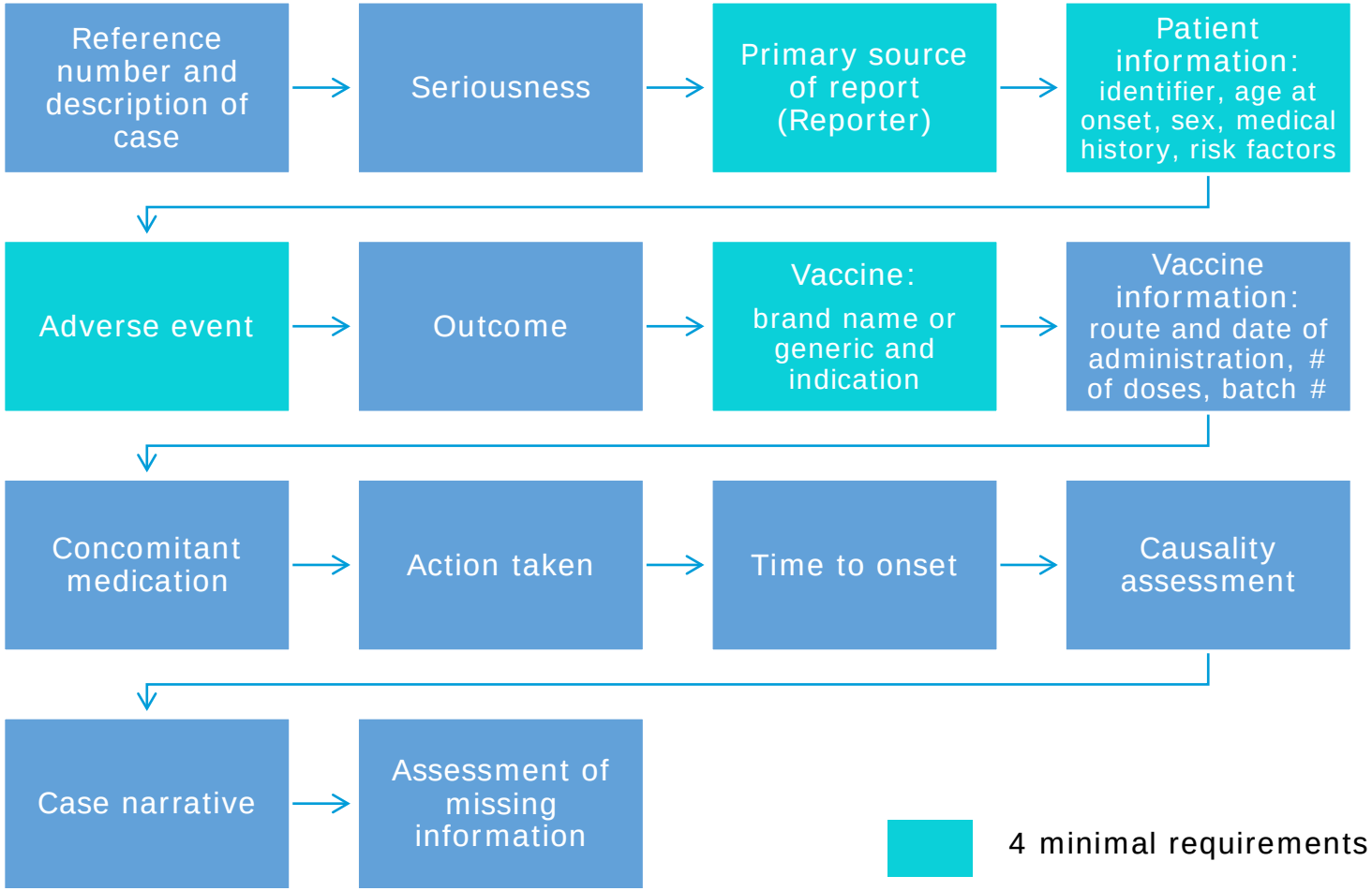
* depending on the PV database system (manual or electronic)

Typical case handling workflow of a safety database system



Automation of PV processes can provide high quality safety data in the correct format, in context, more quickly, and with less manual effort, thereby improving timely scientific assessment.

Essential data for good case quality



THANK YOU

Questions ?