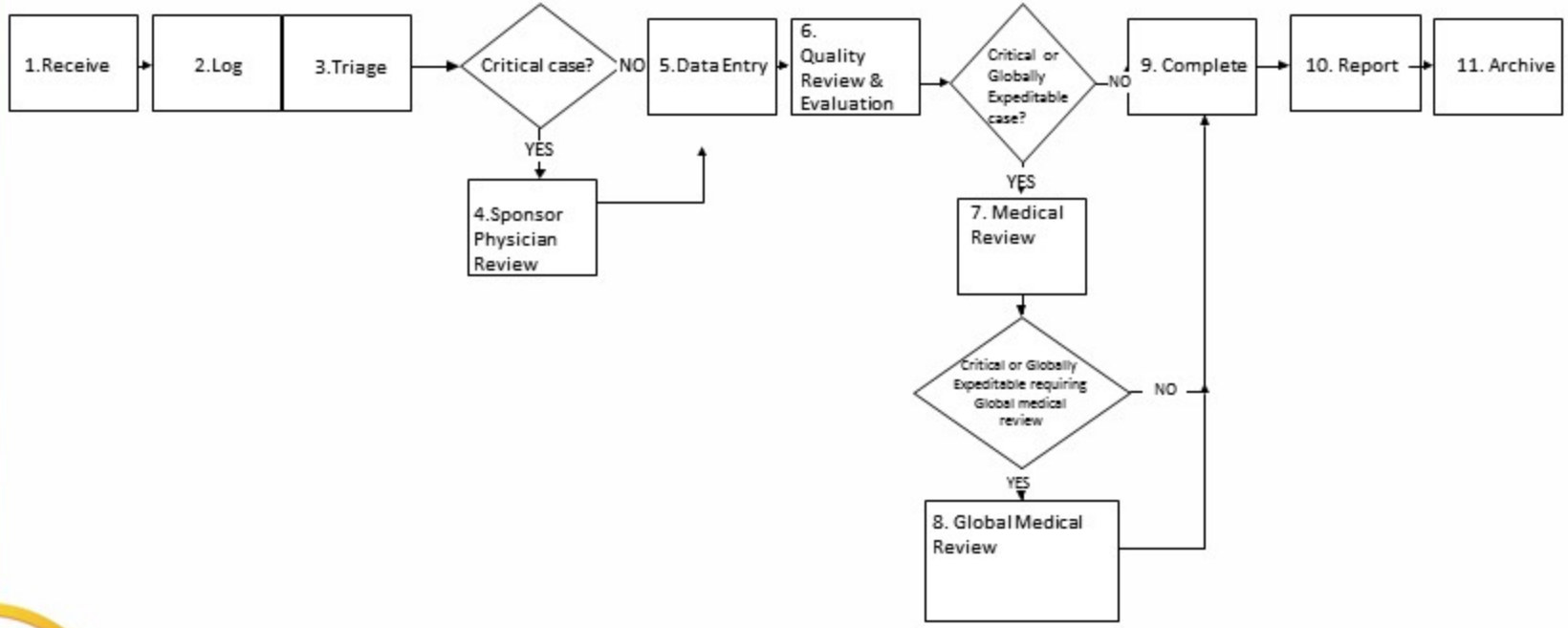
Case Handling Process

Module 9 Topic 3

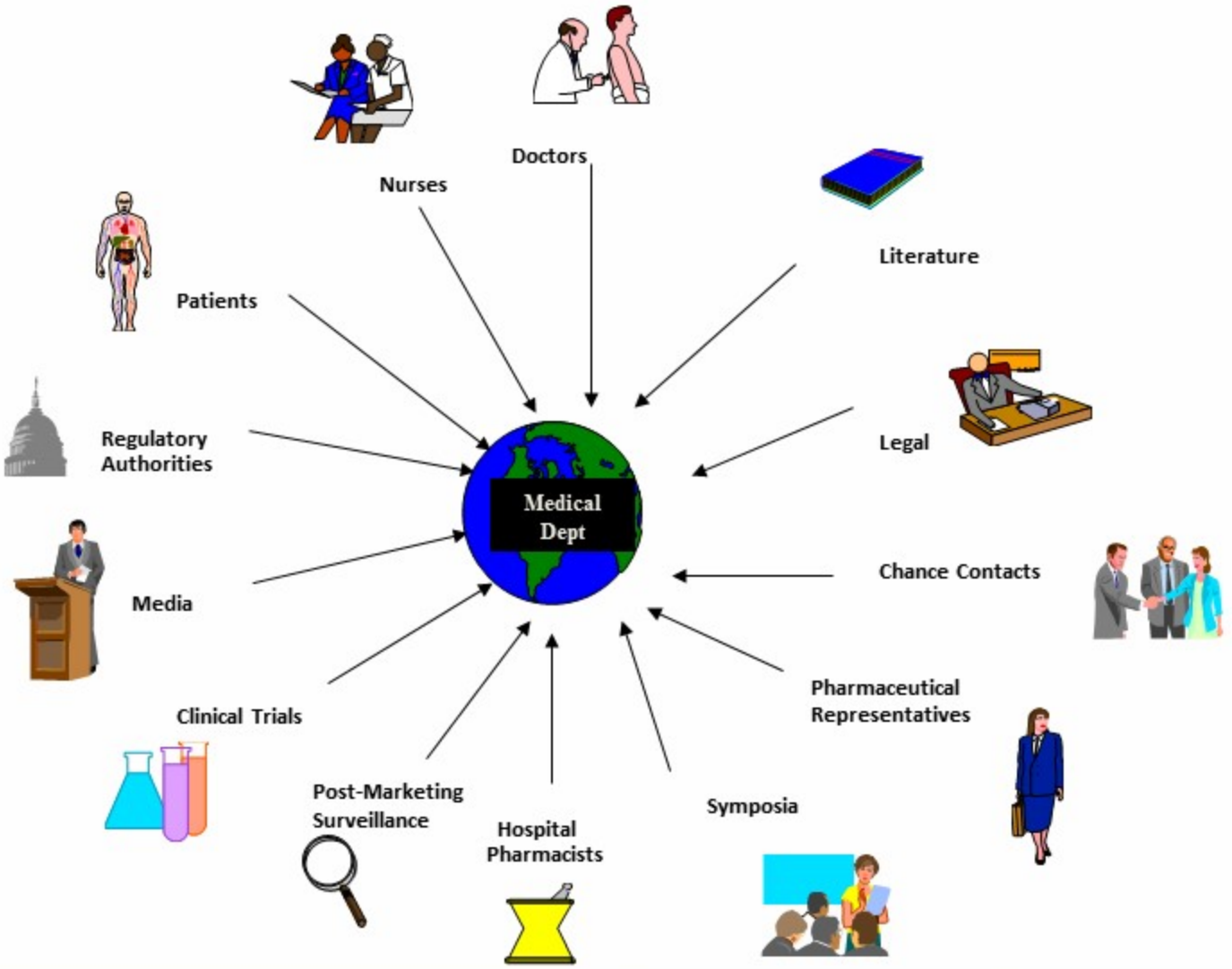
Global Case Handling Process Overview



5 steps in case handling

- AE Occurs
  - Receive
  - Triage
  - Process
  - Review
  - Complete

Sources of AEs



Acknowledgement – Why?

- Encourages further reporting
- Ensures cooperation if more info is wanted
- Builds company image
- Protects the company
- Assists marketing, improves liaison, ensures future prescriptions
- **No acknowledgement = more duplicates**

Triage origins!!!

A process for sorting injured people into groups based on their need for or likely benefit from immediate medical treatment. Triage is used in hospital emergency rooms, on battlefields, and at disaster sites when limited medical resources must be allocated

- (Medicine) the principle or practice of sorting casualties in battle or disaster or other patients into categories of priority for treatment
- (Government, Politics & Diplomacy) the principle or practice of allocating limited resources, as of food or foreign aid, on a basis of expediency rather than according to moral principles or the needs of the recipients

Collins English Dictionary – Complete and Unabridged

Triage

- Assess case for validity as per regulations
- Duplicate search
- Determine regulatory clock start date
- Is the case initial or follow up
- Assess AE terms
- Is the case serious? Expected? Related?
- Is it active or blinded?
- Determine reporting priority
- Send for processing

Duplicate Search

- Common phenomenon
  - Multiple agencies
  - Greater awareness
  - Strict regulations
- Significance to further processing: If follow up, could alter case seriousness & reporting timelines
- Damage potential :
  - Can mislead signal detection systems, improper generation of signals
  - Regulatory action if delayed

Duplicate Search

- Patient, reporter, product , event & permutations
- Patient – identification, location, study
- Reporter – address ,city, street, hospital, HCP/ consumer,
- Change of reporter from consumer to HCP makes case medically confirmed
- Change of info could diminish seriousness of case
- Event – new additions to past report could change seriousness
- Causality – HCP could change his mind about the causality

Case processing

- Assign identification # and assign for data entry
- Perform data entry
- Coding (AE terms, drugs)
- Identify missing case elements
- Follow up for completion
- Prepare narrative
- Review

Data Entry

- Reporter info including street name.
- No patient identifiers as per HIPPA(Health Insurance Portability and Accountability act)
- Generally customised systems have dropdowns of all company formulations; click on the correct formulation (oral, IM,IV, liquid, tablets, caps, SR)
- If company database not up todate – raise flag
- Ensure correct dose is mentioned
- Group cases where needed
- Event data about challenge/ dechallenge, relationship
- **Good DE = good narrative**

Case narrative- Importance

- Provides summary of events to readers who do not have access to original data sets
- Seen/used by various groups
  - case reviewers to decide seriousness, upgrade etc
  - affiliates to triage for their countries,
  - regulatory authorities,
  - during preparation of PSURs and other summary reports
- Essential to follow company & CIOMS guidelines, ensure completeness, chronology and sufficient detail to come to a conclusion
- **It should be ready to be pasted into any report**

Review

- Quality
  - Check for accuracy
  - Check for consistency
  - Check for completeness
- Medical and scientific
  - Confirm triage
  - Check case for medical sense
  - Request non routine follow up if appropriate
  - Make company causality assessment for upgrades or in absence of investigator causality

Medical review (contd)

Appropriateness of the AE terms selected

- Confirmation of the seriousness classification of the AE terms
- Agreement with the listedness/expectedness classification of AE terms, outcome classification. coding of AEs, concomitant conditions, and medical history
- Review of the narrative -it makes clinical sense and includes all important elements

Medical review (contd)

- Authoring the company clinical comment, including determination of the company causality assessment, when appropriate
- Identification of any specific additional information needed for medical assessment purposes other than routine follow-up requests required for case completion
- Upgrade or downgrade to the case's regulatory reportability
- Identification of potential safety signals

A rapid and clearly understood error resolution process must support case review

Drug Safety Physician

Drug-safety physicians are often confronted, especially in relation to spontaneous reporting, with incomplete information on observed adverse events. To make the best use of the information received, they need **medical commonsense, experience** and — when collecting additional information — communication skills.

Drug Safety Physician (contd)

Having collected all the needed information available, the drug-safety physician is supposed to write a **medical evaluation** — including a diagnosis, a **comment on the causal role** of the drug in question, and **alternative explanations**—and a discussion of any action that needs to be taken.

Reporting ADRs, Clinical Terms & Definitions for their use. CIOMS handbook,1999

Single Case Assessment

- Only SAEs
- CIOMS review
- Narrative checking
- Medical Cohesiveness
- Lab data that could be ADR
- Causality

Can he remember cases? Can he see trends?

Case completion

- Case reviewed
- Incorporate requested changes
- Request expedited report (if required) with attachments & supporting correspondence
- Distribute globally
- Produce and forward expedited report (if reqd)
  - Send to reg authorities as apropriate
  - Circulate to internal company personnel
  - Send to external partners (licencees, distributors)
- Generate requested followup (if required)
- Archieve case

Why perfect reporting? Flupirtine

- Flupirtine, a centrally acting non-opioid analgesic
- Suspition of liver related injury
- Study re-evaluated the plausibility and causality of 226 unselected, spontaneously reported hepatobiliary ADRs
- Only 20% of the reported cases were probable or likely for F treatment, suggesting an incidence of F-related liver injury of 1: 100,000 when estimated prescription data are considered, or 0.8 in 10,000 on the basis of all 226 reported ADRs

Why perfect reporting? Flupirtine (contd)

- In 151/226, an average of 3 comedications with drugs known for their liver liability were observed. These may well be causative for ADRs,but were reported under a suspected flupirtine ADR
- Need to improve the quality and standards of ADR reporting

Anderson, Borlak, PLoS ONE, October 2011,6: e25221

Line listings

- Should include each subject only once
- If more than one ADR, they should all be mentioned but listed under the most serious ADR, as judged by the sponsor

Line listings (contd)

- If the same subject experiences different ADRs on different occasions, such experiences should be be treated as separate reports
  - Same subject might then be included in a line listing more than once
  - Line listings should be cross-referenced when possible
- Cases should be tabulated by body system (standard system organ classification scheme)
- Usually one listing for each trial - separate listings may be provided when appropriate and relevant

Content of line listing (1)

- Clinical trial identification
- Study subject's identification number in the trial
- Case reference number in the sponsor's safety database for medicinal products
- Country in which case occurred
- Age and sex of trial subject
- Daily dose of investigational medicinal product; dosage form and/or route of administration, when relevant
- Date of onset of reaction, or estimate of time to onset from therapy initiation if date not available; for ADR known to occur after cessation of therapy, estimate of time lag if possible

Content of line listing (2)

- Dates of treatment, or estimate of treatment duration if dates not available
- Adverse reaction: description of reaction as reported; when necessary, also as interpreted by the sponsor
  - Where medically appropriate, signs and symptoms can be lumped into diagnoses
  - MedDRA should be used
- Patient outcome
  - Resolved, fatal, improved, sequelae, unknown
  - Should indicate consequences of the reaction(s) for the patient, using the worst of the different outcomes for multiple reactions

Content of line listing (3)

- Comments, if relevant e.g.:
  - Causality assessment if sponsor disagrees with the reporter
  - Concomitant medications suspected to play a role in the reactions
  - Indication treated with the suspect drug(s)
  - Dechallenge/rechallenge results if available
- Unblinding results in the case of unblinded SUSARs
- Expectedness as at the time of the occurrence of the suspected SARs, assessed with the reference document in force at the beginning of the period covered by the report

Good reporting – leads to

- Good narrative in PSUR
- Good collation and segregation of data for review
- Signal detection
- Patient safety