INTRODUCTION TO PHARMACOVIGILANCE

Revisions and Approval

Author	Document ID	Version	Date	Change description
Vandana Tanwar	RX-TRN-BUS-001	Version 4.0	6-Apr-2020	Reviewed and no changes in the content of the training material.
Deepika Dubey	RX-TRN-BUS-001	Version 3.0	8-Mar-2018	Addition of Regulatory Reporting
Bhavana Pant	RX-TRN-BUS-001	Version 2.0	31-May-2016	Addition of Training assessment section
Bhavana Pant	RX-TRN-BUS-001	Version 1.0	01-Feb-2016	N/A

Agenda

- Pharmaceutical Industry
- What is a Drug?
- Why we need Drugs?
- Drug development lifecycle
- Need of Clinical Research
- Clinical Trials – Phases
- Clinical Trials –Business process
- Limitations of Clinical Trials
- What is PV
- History of PV
- Need of PV
- Safety business process
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- Types of Regulatory Reporting

Pharmaceutical Industry

- Develops, produces, and markets drugs or pharmaceuticals licensed for use as medications
- What makes this industry unique is:
  - *Research*
    - Drug discovery is the process by which potential drugs are discovered or designed
  - *Regulations*
    - Laws and regulations regarding the patenting, testing and ensuring safety and efficacy and marketing of drugs
  - *Ethics*
    - Healthcare is in a unique position balancing profit and the public good
  - *Economics*
    - **Largest of any industry**
    - in 2014, global spending on prescription drugs topped $1 Trillion and seen at 1.5 trillion in 2021.
    - US is the Largest market – 1/3rd of global pharmaceutical market($374 billion in annual sales)

What is a Drug?

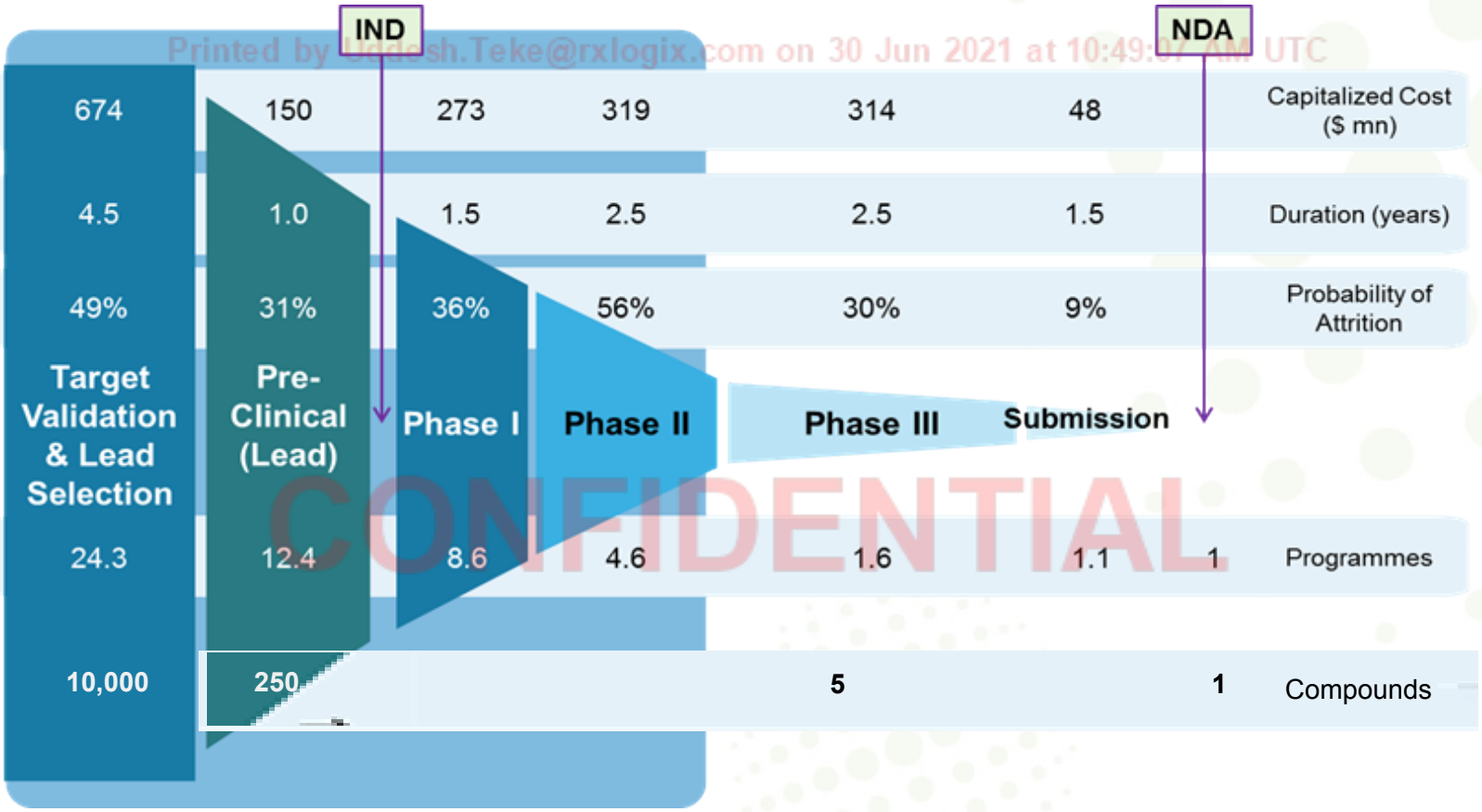
- *A substance that has known biological effects on humans or animals*
- Formal Definition
  - a substance used in the treatment, cure, prevention, or diagnosis of disease or used to otherwise enhance physical or mental well-being
- Dispensing of medication is often regulated by governments into three categories
  - *Over-the-counter (OTC) medications*: available in pharmacies and supermarkets without special restrictions
  - *Behind-the-counter (BTC):* which are dispensed by a pharmacist without needing a doctor's prescription
  - *Prescription only medicines (POM):* which must be prescribed by a licensed medical professional, usually a physician

Why we need Drugs?

- Why we need drugs:
  - Treatment of disease
  - Diagnosis of a disease
  - Prevention of a disease
  - Enhance body function
- A disease is a particular abnormal condition, a disorder of a structure or function, that affects part or all of an organism. Disease is often construed as a medical condition associated with specific symptoms and signs. It can be
  - Pathogenic (infection)
  - Hereditary (genetic disorder)
  - Deficiency (malnourishment)
  - Physiological (asthma, stress)

Drug development Life Cycle

- This is a risky, expensive, lengthy and highly regulated process



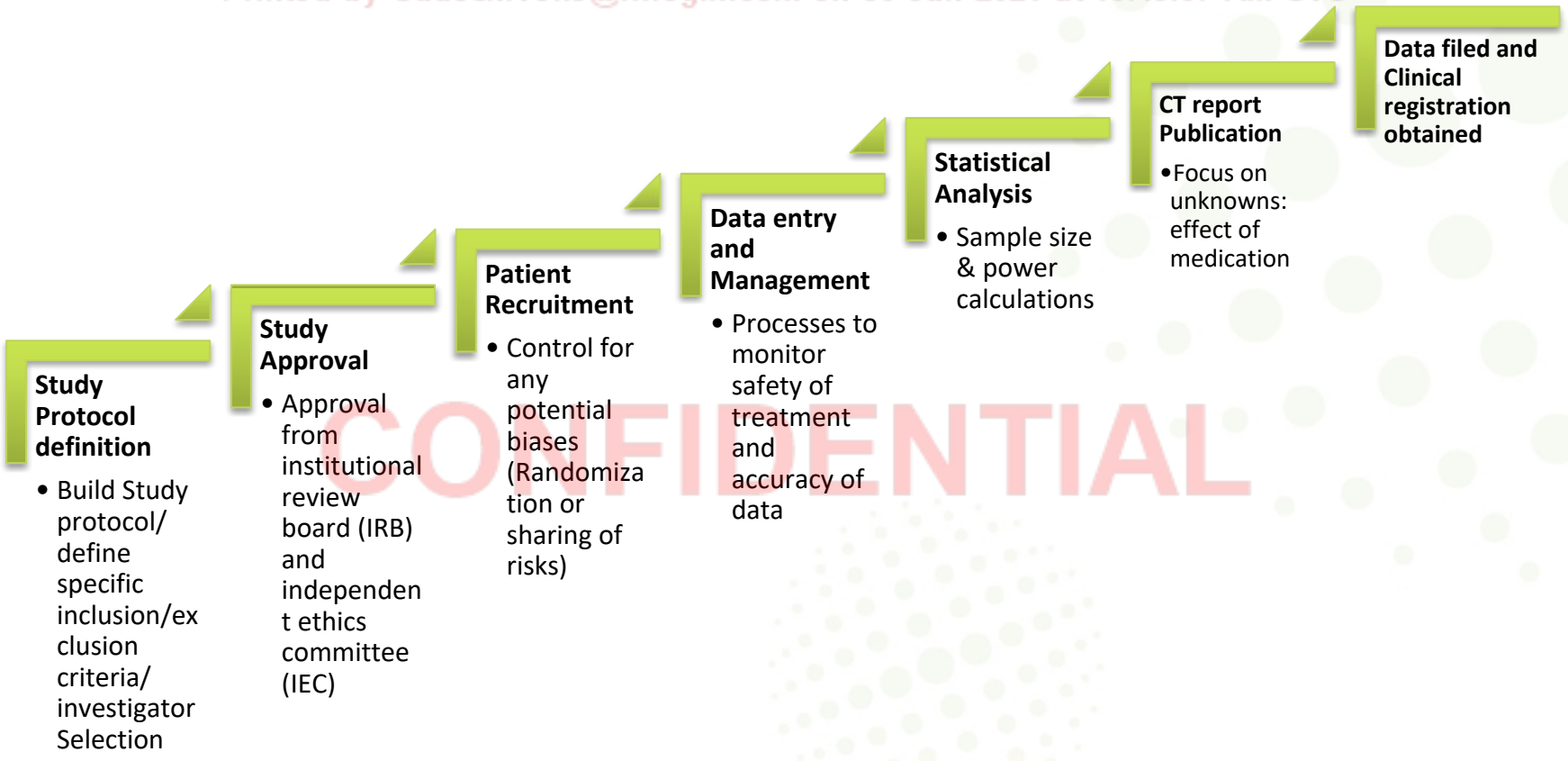
Need of Clinical Research

- Animal experiments have limited value in predicting human safety and efficacy so additional research is required.
- Clinical Research helps in:
  - **Safety and Efficacy** assessment
    - of an experimental therapy on a specific disease
    - of a different dose of a medication than is commonly used
    - of an already marketed intervention for a new indication
  - **Comparing the efficacy** of two standard or marketed interventions
  - Evaluation of the **new therapy in comparison to standard therapy**

Clinical Trials – Phases

Phase	Number Of Participants	Duration	Purpose
Phase I	20-100 Healthy volunteers	6-12 months	SAFETY Tolerability *Drug developers, or sponsors, must submit an Investigational New Drug (IND) application to FDA before beginning clinical research*
Phase II	100-300 Patients	6-36 months	EFFICACY Dose-ranging/finding Preliminary efficacy and Tolerability
Phase III	200-1000 Patients	1-5 years	THERAPEUTIC VALUE Long-term safety and efficacy v/s competition drugs *The NDA application is submitted to FDA through which drug sponsors formally propose for approval of new pharmaceutical for sale and marketing*
Phase IV	Unlimited Patients	5 years post-market release	PMS (Post Marketing Surveillance) Drug Surveillance, after Marketing license Submission to regulatory authority

Clinical Trials – Business process



Limitations of Clinical trials

- Clinical trials are only a *proof-of-concept* but not an actual representation of the drug action on the entire human population as they are *limited in time and number of patients*
- Subjects in trials are 'Perfect patients', selected as they have no other diseases/ are not on other medications/ pregnant/ elderly
- Rare or delayed serious reactions are likely to remain unnoticed as the trial duration is too small to determine
  - Drug-drug interactions
  - Drug-disease interactions
  - Drug-demographic interactions

What is PV

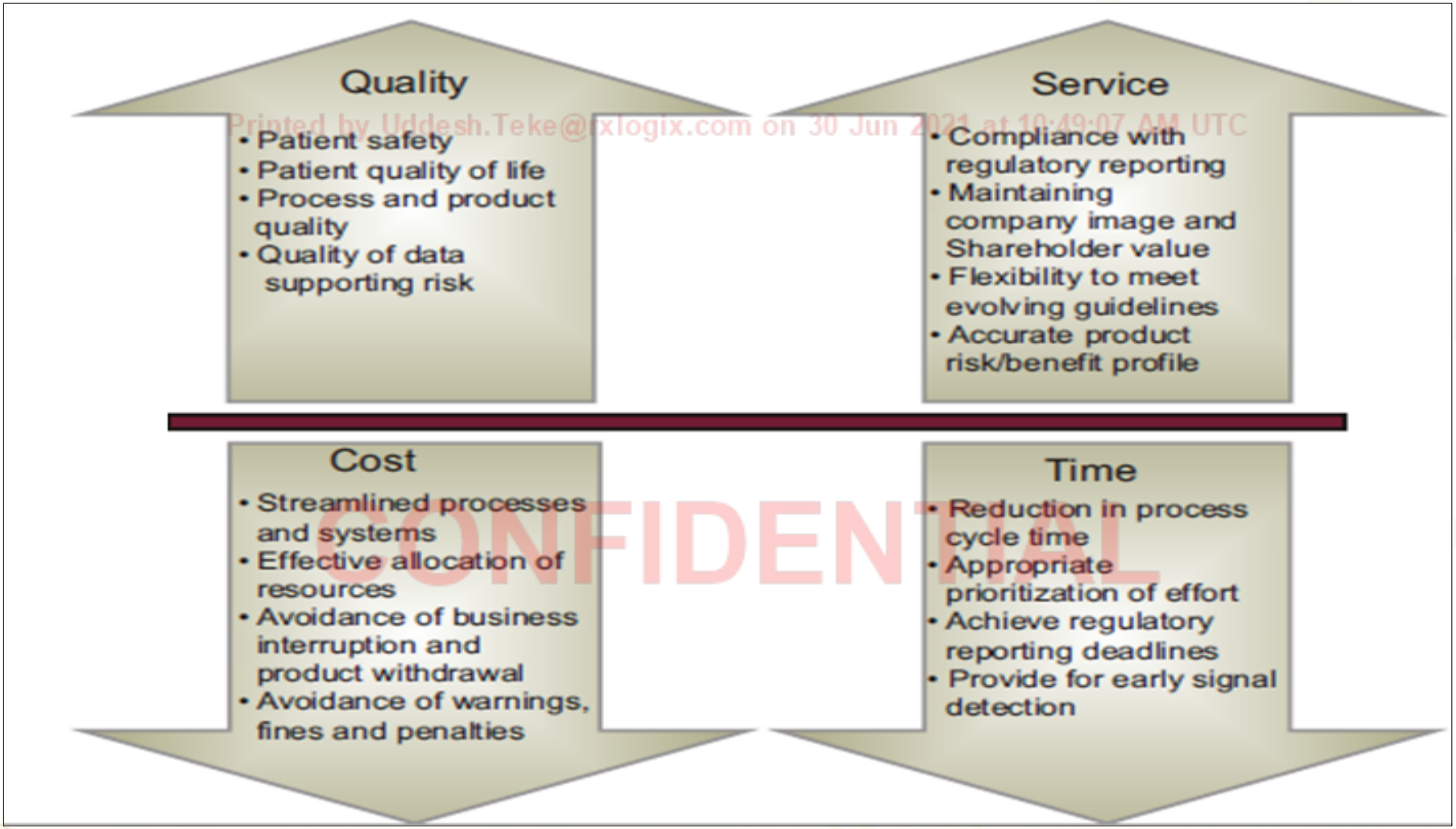
- **WHO Definition:** Pharmacovigilance (PV) is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem
  - *Together with the WHO Collaborating Centre for International Drug Monitoring, Uppsala WHO promotes PV at the country level (WHO-UMC). At the end of 2010, 134 countries were part of the WHO PV Programme*.
- PV is undertaken to continuously monitor and evaluate product risk-benefit in an ongoing manner
- For early signal detection - quickly identify new medical risks to patients
- To provide optimal prescribing information and advice
- To comply with regulations, reporting timelines and regulator expectations. To avoid warnings, fines or penalties
- To avoid product liability and legal costs
- To avoid business interruption and product withdrawal

History of PV

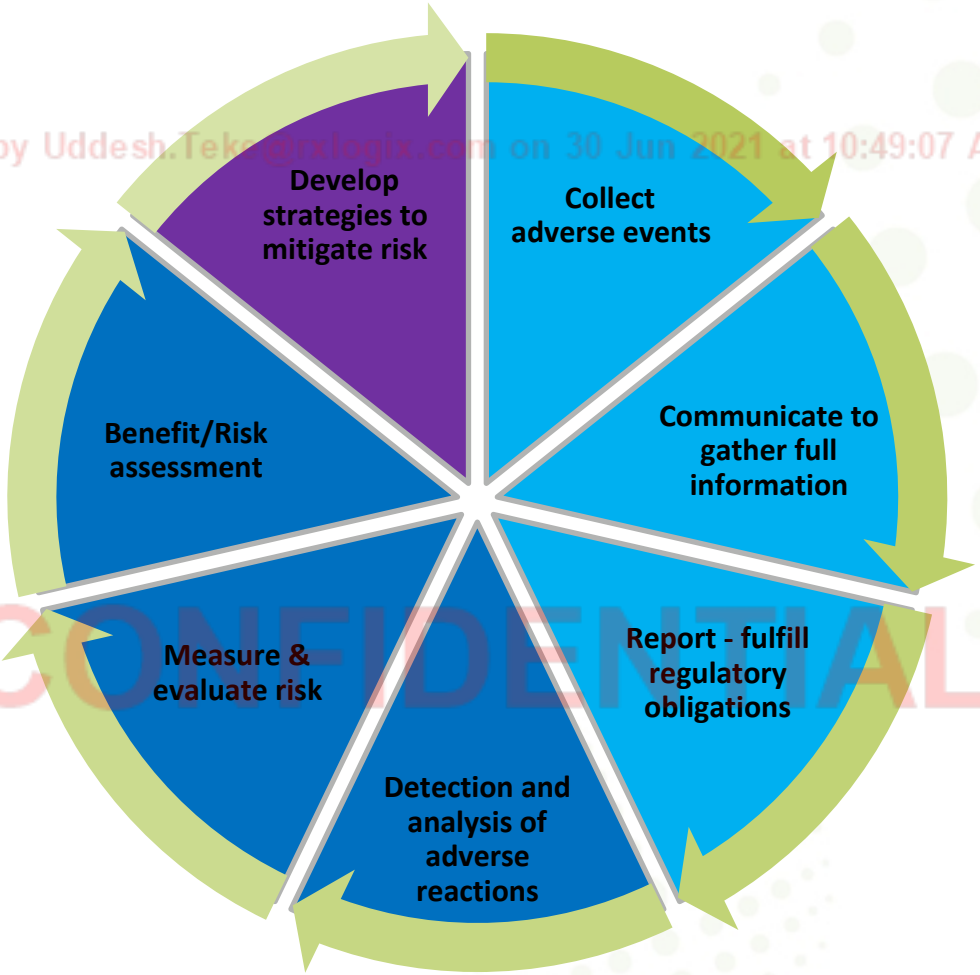
- Thalidomide used by thousands of pregnant women between 1957 and 1961 for morning sickness
- One of the biggest medical tragedies of modern times – a potent teratogen which caused limb deformities in over 10,000 victims in 46 countries

- Led to our current drug approval process and PV regulations
- Dr. Frances Kelsey at FDA blocked sales in the US and received a prestigious award
- Withdrawn from the market in 1961
- Came back in market in 1998 for treatment of lesions due to leprosy and in 2006 approved by the FDA for multiple myeloma under tightly controlled conditions for use

Need of PV

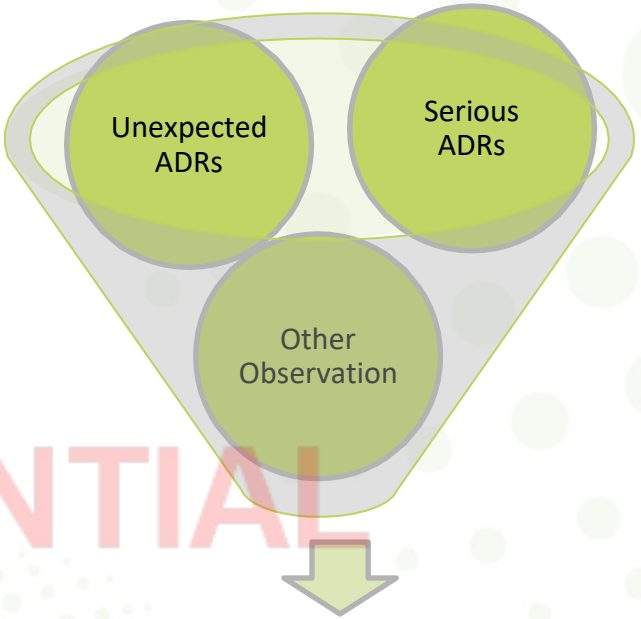


PV Process



Reporting

- Minimum Criteria For Reporting
  - Identifiable patient
  - Suspect medicinal product
  - Identifiable reporting source
  - In event or outcome, that can be identified as serious and unexpected, and for which, in clinical investigation cases, there is a reasonable suspected causal relationship
- Follow-up information should be actively sought and submitted as it becomes available



Types of Regulatory Reporting

- **Expedited Reporting:**
  - This refers to ICSRs (individual case safety reports) that involve a serious and unlisted event (an event not described in the drug's labeling) that is considered related to the use of the drug.
  - In most countries, the timeframe for reporting expedited cases is 7/15 calendar days from the time a drug company receives notification
- **Aggregate reporting**
  - also known as periodic reporting, plays a key role in the safety assessment of drugs. Aggregate reporting involves the compilation of safety data for a drug over a prolonged period of time (months or years), as opposed to single-case reporting which, by definition, involves only individual AE reports.
  - The advantage of aggregate reporting is that it provides a broader view of the safety profile of a drug. Worldwide, the most important aggregate report is the Periodic Safety Update Report (PSUR) and Development safety updated report (DSUR).

Thank you

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