Syneos Health:

An Inside Look at the world's first CRO and CCO

Introductions: Who are we?

Ryan Sarda

Sr. Talent Acquisition Specialist: North America recruitment lead for Medical Affairs, TMF Operations, and Site andPatient Access.

Octavio Hernandez

Talent Acquisition Specialist: North America recruitment lead for Safety & Pharmacovigilance, Study Start-Up & Regulatory and Site Contracts.

Jodi List

Manager Safety & Pharmacovigilance

What is a CRO?

A Contract Research Organization (CRO) is a service organization that provides support to the pharmaceutical and biotechnology industries in the form of outsourced pharmaceutical research services (for both drugs and medical devices).

Syneos Health provides end-to-end pharmaceutical research in Phases I-IV for many clinical trials in:

- Clinical Development (TBUs)
  - Central Nervous System
  - General Medicine
  - Oncology
- Clinical Development Services
- Early Phase
- Real World & Late Phase
- Strategic Alliance Management

Who is Syneos Health and what sets us apart from our competitors?

Syneos Health is an end-to-end fully integrated CRO and CCO (Contract Commercial Organization) that strives to bring new therapies to market faster than before

- Product of a merger between INC Research and inVentiv Health, became Syneos Health in January 2018
  - 23,000+ employees worldwide
  - 1,800+ studies worldwide
  - 87,000+ sites worldwide
  - 553,000+ patients worldwide

- Only CRO and CCO in the industry
  - Biopharmaceutical Accelerator Model (BAM!)
    - Clinical and Commercial work together and constantly share real world knowledge and insights that lead to getting the job done better, smarter and faster

Multiple executives selected to the PharmaTimes International Clinical Researcher of the Year 2018 including five recipients in 2018

Learning Solutions from Syneos Health named to the Training Industry's Top Content Development Companies Watch List in 2018

Awarded the Society for Clinical Research Sites (SCRS) Eagle Award in the CRO category for superior leadership and commitment to sites in 2018 and 2017

Listed as one of the top five companies for Work-from-Anywhere Remote Jobs in the U.S. in 2018

Multiple executives awarded PharmaTimes' Clinical Research of the Year including Julie Locke in 2016 and Stephanie Rogg in 2018

Recognized by Virtual Vocations as one of the top 100 telecommuting companies in 2018

Syneos Health: A CRO with a true global footprint

More than 23,000 employees with experience spanning six continents, including trials of any size and scope

Syneos Health: Globally Headquartered in Morrisville, NC

New Morrisville, NC Headquarters

- Consolidated **4** offices in the Raleigh area and built a brand new state of the art facility in Perimeter Park
- About 1,400 employees are based in the new building currently with plenty of room to add more due to growth and expansion of the organization
- Move to new HQ was completed in January 2019

Syneos Health is hiring for employees just like you!

- Medical Affairs
  - Medical Directors, Medical Operations, Medical Scientists
- Trial Master File Operations
  - Document Management, Regulatory Records
- Site Start-Up
  - Site Contracts, Regulatory Documents
- Patient Engagement
  - Site Intelligence, Patient Recruitment
- Safety and Pharmacovigilance
  - Safety Data Coordinators, Safety Submissions Specialists, Safety Specialists, Safety Physicians)

Pharmacovigilance Overview

Jodi List RN, BSN, Manager Safety & Pharmacovigilance

Agenda

- Definitions
- What is Pharmacovigilance
- Event Assessment
- Determining Reportability
- Identifying and Describing Safety Signals
- Post-Marketing Surveillance

Definition

- Pharmacovigilance:
  - Involves all scientific and data gathering activities relating to the detection, assessment, and prevention of adverse effects or any other drug related problems.
  - The goal of these activities is to identify adverse events and understand, their nature, frequency, and potential risk factors.

Definitions

- **What is an AE?**

- An **Adverse Event (AE)** or Adverse Experience is defined as:

*"Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment" (**ICH E2A: Clinical Safety Data Management)***

- **What is an ADR?**

- An **Adverse Drug Reaction (ADR)** is *"any response to a drug which is noxious and unintended and that occurs at doses used in man for prophylaxis, diagnosis or therapy".*

Definitions

- **What is an SAE?**

- A **Serious Adverse Event (SAE)** or Serious Adverse Experience is any untoward medical occurrence that at any dose:
  - Results in death
  - Is life-threatening
  - Requires inpatient hospitalization or prolongation of existing hospitalization
  - Results in persistent or significant disability/incapacity
  - Is a congenital anomaly/birth defect
  - Is an important medical event.

- **Serious vs Severe:**
  - A headache can be **severe** but not require hospitalization (**non-serious**)
  - A mild heart attack could still be life threatening (**serious**)

Definitions

What is a SUSAR?

- A **SUSAR** is a **S**uspected **U**nexpected **S**erious **A**dverse **R**eaction or
- A **Serious Adverse Event** that is **suspected** to have a causal relationship with the medicinal product under investigation, the severity is not consistent with information in the relevant product literature (such as the Investigator's Brochure or Patient Information Leaflet) and is considered to be **unexpected**

- **SUSARs** must be submitted in **expedited** manner to
  - Regulatory Authorities
  - Ethics Committees (ECs)/ Independent Review Boards (IRBs)
  - Investigators

- **Reason:** To provide new important information on serious adverse reactions

What is Pharmacovigilance?

- The decision to approve a drug is based on having a satisfactory balance of benefits and risks within the conditions specified in the product labeling.

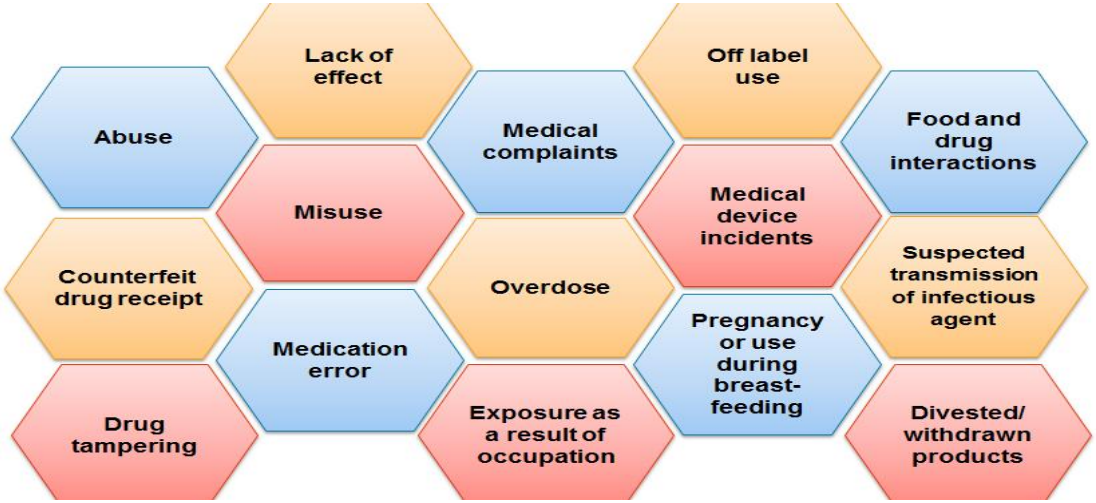
- The knowledge related to the safety profile of the product can change over time through expanded use and the number of patients exposed to the product.

	Phase I	Phase II	Phase III	Phase IV
Test size	20-80	100-300	Several hundred to several thousands	TBD
Condition	• Healthy	• Have particular condition • Meet other trial requirements	• Have particular condition • Meet other trial requirements	• Have particular condition • Meet other trial requirements
Objective of test	• Determine drug's basic safety data	• Dose ranging studies • Determine drug's relative safety and efficacy at different doses	• Significant safety and efficacy in comparison with placebo or standard of care	• Monitor long-term risks and benefits • Evaluate different safety and efficacy parameters
Typical duration	• 6 months to 1 year • Comprised of numerous clinical trials of short duration	• Average of 1 to 2 years • Comprised of several longer duration clinical trials	• Generally last up to 3 years	• Conducted after drug approval • Post-marketing surveillance required by health authorities

What is Pharmacovigilance?

- Once a product is marketed, new information will be obtained, which can have an impact on the benefit-risk balance of the product.

- In collaboration with regulatory agencies, the new information should be continuously evaluated in order to ensure that the product is safe to use.



What is Pharmacovigilance?

Collate

- Responsible for facilitating the collection of data in order to monitor the safety of patients enrolled in clinical trials and during post marketing

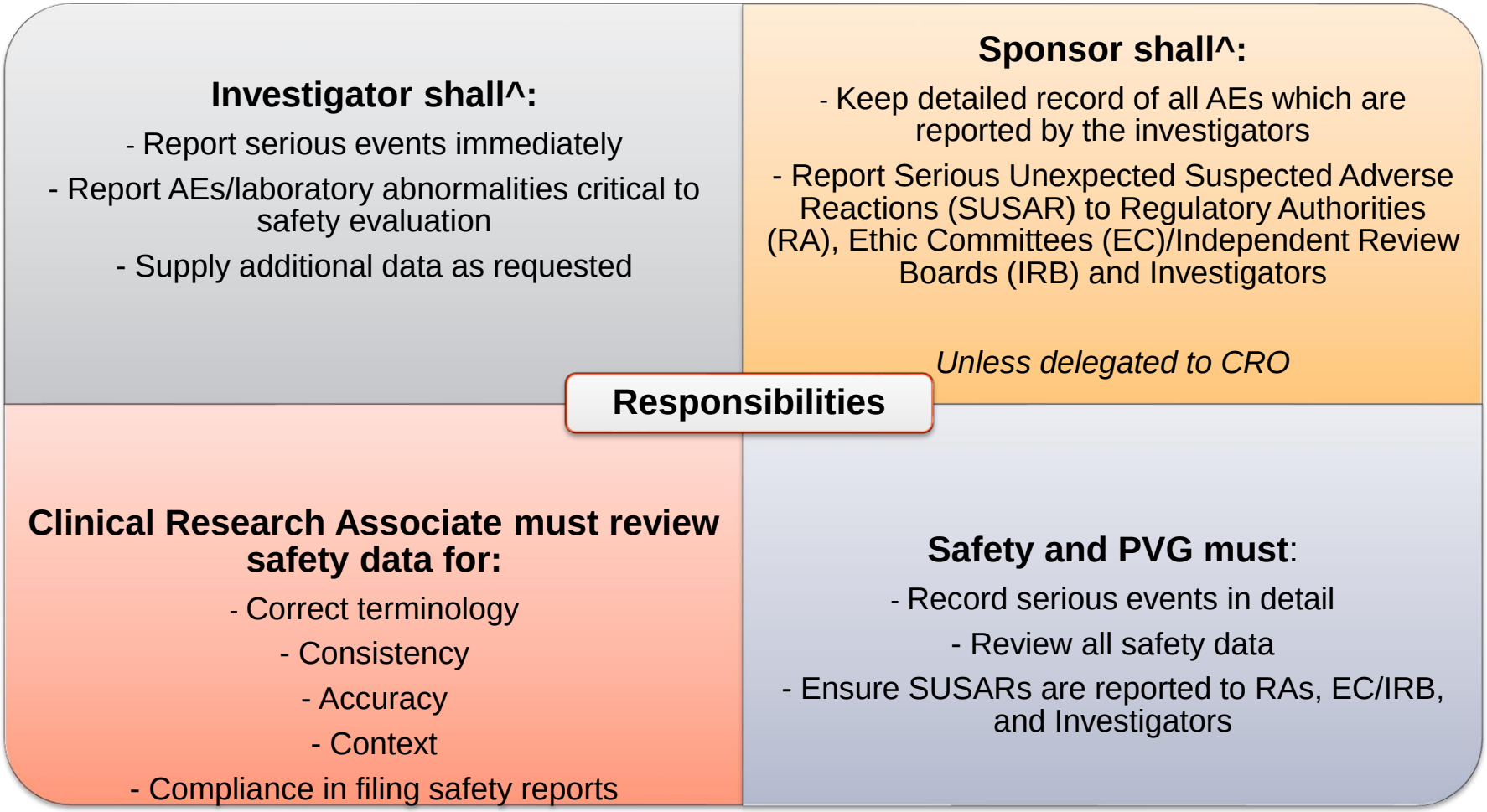
Analyse

- Analyse the data to provide constant assessment of the benefit-risk ratio/profile of the medicinal product in clinical trials and post marketing

Report

- Report individual cases and other reports and assessments to regulatory authorities and justify both benefit-risk profile of the product and the safety system assessing it to all competent authorities

Responsibilities of Key Parties



Adverse Event Assessment

- The expectedness of an adverse event is determined by referencing the current product labelling (such as the Investigator's Brochure or Patient Information Leaflet).

- Adverse events listed in the current labelling are considered expected.

- Adverse events are considered ***unexpected*** if they meet any of the following criteria:

  1. The event is not listed in the current product labelling.
  2. The nature of the event differs from the information in the current product labelling.
  3. The event differs in specificity as described in the current product labelling.
  4. The event is reported with greater severity than described in the current product labelling.

Determining Expectedness

Examples:

1. Hepatic necrosis would be unexpected if the labelling only referred to elevated hepatic enzymes or hepatitis.

2. Cerebral thromboembolism and cerebral vasculitis would be unexpected if the labelling only listed cerebral vascular accidents.

3. Even though pulmonary embolism is listed on the product labelling, a pulmonary embolism that resulted in death would be considered unexpected if the labelling did not specifically indicate that a patient could die as a result of the event.

Determining Reportability

- The reportability of a case is based on the seriousness and the expectedness of each adverse event reported.

- The regulatory authorities guidelines for seriousness and expectedness are applied for each adverse event (FDA, etc.).

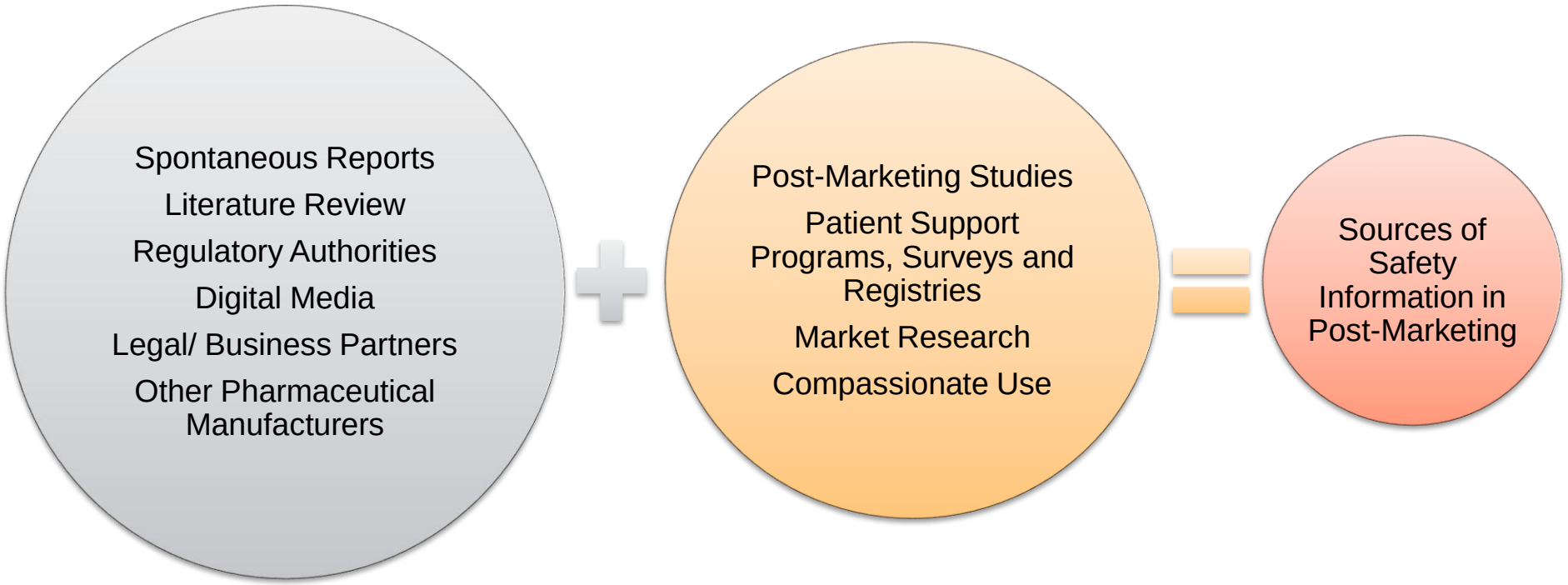
Determining Reportability

- After evaluating each adverse event for seriousness and expectedness, the type of report is determined and the timelines for submission are applied as follows:
  - 7-Day Notification
  - 15-Day Alert Reports
  - Serious and expected reports
  - Non-serious and expected/unexpected reports

Identifying and Describing Safety Signals

- In assessing case reports, the FDA suggests that sponsors evaluate the causal relationship between the product and the adverse event, including:
  - Occurrence of the adverse event in the expected time
  - Absence of symptoms related to the event prior to exposure
  - De-challenge and Re-challenge (what happened when the drug was stopped/what happened when the drug was re-started)

Sources of Safety Information in Post-Marketing



Important: Unlike clinical trials, **all employees**, contractors and affiliates of the marketing authorization holder/manufacturer are obliged to report all safety information they became aware of anywhere (including IT, cleaning staff etc).

Maintaining Patient Safety

When asked what I do for a living, I always tell people:

"you know those little leaflets you get inside a box of Tylenol, that lists the possible side effects…..my team collects and reviews the data that is used to write those."

Syneos Health

Any Questions?

Shortening the Distance From Lab to Life™

Syneos™ Health