Module-8

Signal Detection:

**Definition:** Information arising from one or multiple sources, including observations and experiments, which suggests a new potentially causal association, or a new aspect of a known association between an intervention and an event or set of related events, either adverse or beneficial, that is judged to be of sufficient likelihood to justify verificatory action [IR Art 19(1)].

The Process of signal detection:

Sources of signal:

**Signal detection:**

The Signal detection can be done through:

* ICSRs (individual case safety reports)
* Statistical analysis
* Both ICSRs & Statistical Analysis.

The process is selected based on the volume of cases the marketing authorization holder receives the cases. If the volume is low, it will be ICSRs and if the volume is more the statistical analysis is opted and sometimes both as required.

**Signal validation:**

The validation depends on:

1. The signal identified is compared with the product information whether it is known or new event or it is monitoring through PSUR or mentioned in RMP.
2. Any information available in the literature search and database of the MAH (Strength of association).
3. Any other additional information available in the clinical data, information from authorities, information from the same class of drugs.

As per the EMA after validation:

Signal can be validated signal or non-validated signal.

Validated signal can be refuted based on the available information and can be refuted if no sufficient data available to support the signal.

**Signal analysis and Prioritization:**

A validated signal with new information or increased known information is further analyzed with any spontaneous cases available in database or spontaneous data in Eudravigilance (by European authorities), any recent literature information, information available from health care professionals regarding the signal and communicated to the MAH to collect the information further in speculated timelines.

**Signal Assessment:**

Based on the information provided by MAH and the data obtained by the authorities, the decision will be finalized.

It can be a Regulatory action with:

1. Update the labels as variation provided.
2. It can be an additional risk minimization measure and advised to go for Direct health care professions communications (DHPC).
3. Can initiate the referral procedure.

**PRAC**- Pharmacovigilance risk assessment committee is the authority from European medical agency which manages the signal management.

**Emerging safety issue:**

During the review of signal process, if there is any information which impacts the safety of the public health and major or potential risk to the public health it will be considered as Emerging safety issue and to notified to the authorities within three days.

Standalone notification:

The information from the signal review which does not have major risk to the public health can be provided to the authorities within 6 months .

The timelines are provided as per the GVP module IX.

**Signal management process:**

Individual case safety reports

Clinical trials

Literature reports

Signal Detection in AE reporting System