Journal of Pharmacovigilance
ISSN: 2329-6887

Garlapati and Priyanka, J Pharmacovigil 2014, 3:1
DOI: 10.4172/2329-6887.1000e126

Editorial Open Access

# Cradles of Signals for Pharmacovigilance Process

**Suman Garlapati**[1*] **and Shanthi Priyanka**[2]

[1]*Drug Safety & Pharmacovigilance Officer, Invagen Pharmaceuticals, New York, USA*

[2]*Vigilare Biopharma, Pvt. Ltd. Kukatpally, Hyderabad, India*

[*]**Corresponding author:** Suman Garlapati, Drug Safety & Pharmacovigilance Officer, Invagen Pharmaceuticals, New York, USA, Tel: 1-914-486-1898; E-mail: suman1981@gmail.com

**Rec date:** Dec 18, 2014; **Acc date:** Dec 18, 2014; **Pub date:** Dec 25, 2014



## Editorial

Adverse effects are manifold and diverse. Pharmacovigilance and signal detection are the lifetime activities to do for a drug (both pre and post marketing) to determine adverse events & to suggest a new potentially causal association or a new aspect of a known association. Anything which is new is considered as signal, it should be validated taking into account other relevant sources of information.

## Signal Detection

### The WHO defines a safety signal as

"Reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously" [1]. Usually more than a single report is required to generate a signal, depending upon the event and quality of the reports available. When a signal is detected, further investigation is warranted to determine whether an actual causal relationship exists.

## Signal Detection Tools

Single cases, aggregated data, literatures, databases

## Sources of Signal Detection

The sources for identifying new signals are diverse. They potentially include all scientific information concerning the use of authorized medicinal products including quality, non-clinical, clinical and pharmacovigilance data. Sources for signals include spontaneous reporting systems, active surveillance systems, non-interventional studies, clinical trials and other sources of information.

Spontaneous reports of adverse reactions may be notified to pharmacovigilance systems, poison centers, teratology information services, and vaccine surveillance programs.

Signals in pharmacovigilance are usually derived from studies/ post market survilliers or experiments. They have both quantitative and qualitative aspects [2].

In case of qualitative reports ,single case may be a valid signal depending on the nature of the effect, quality of reports ,consistency of data ,biological plausibility of drug, previous experiences with the drug, time relatedness and possible evidence from other sources. Qualitative signals mainly concerns about the number of case reports and statistical considerations.

Marketing authorization holders should check internet or digital media under their management for potential adverse effects which may characterize a new signal

Important data which helps in finding signals are recent reports, dechallenge, rechallange, time relationship, geographical evaluation [3], biological plausibility, informative reports.

### Qualitative signals

Spontaneous reports, Literature reports, Intensive hospital monitoring, Prescription event monitoring, Follow-up studies.

### Quantitative signals

Large data resources, Case control studies, Intensive hospital monitoring, and Prescription event monitoring, Follow-up studies.

### Experimental

- Clinical trials, Animal studies.

### Quantitative strength of the association

- Number of individual case reports
- Statistical disproportionality

### Consistency of the data (pattern)

- Exposure-response relationship
- Site, timing, dose, reversibility
- Biological plausibility of hypothesis
- Pharmacological, pathological

### Experimental findings

- e.g. dechallenge, rechallange, blood levels, metabolites, drug-dependent antibodies

### Nature and quality of the data

- Objectivity, documentation, causality assessment

Three main sources of evidence for drug safety [4]:

–Controlled clinical trials –epidemiological studies –Statistical analysis

Besides the traditional review of spontaneous cases and other safety information by trained medical personnel, "data mining" [5] may also be carried out. This is the process of applying sophisticated statistical

algorithms to large safety databases to determine whether certain adverse events (AEs) are being reported for a medicine with a greater frequency than expected (i.e., a signal of disproportionate reporting [6], or SDR), based on a statistical model. Statistical methods and epidemiological methods are mainly used to for large amount of datasets.

## Discussion

Earlier there are no sophisticated data collection systems for adverse drug effects reporting. Now a days it's a major concern to report the drug related adverse effects for the better life of the public and the drug. Drug starts with absolute no adverse events. As the drug passes through development process and post market application, adverse effects starts appearing. Then pharmacovigilance and signal mechanism comes into picture to collect, detect, analyze, report and treatment of adverse drug effects.

The relation between drug and event is difficult to finalize because of complex, confounding factors. It requires varied data from spontaneous reports, non-clinical, clinical trial reports to know the pharmacological effects of drug and its effects in human beings, data from market authorization holders to know the post authorization history of the drug. Different adverse effects require different methods of signal detection. Besides varied data expertise and better understanding of scientific methods is necessary for rationale decision making in pharmacovigilance and signal detection. Although statistics deal with large amount of data, it's the medical and scientific judgment of expert pharmacovigilance professions decision makes the priority. For this decision making various sources are necessary.

## Conclusion

Signals in pharmacovigilance have variety of sources. A better understanding of signal detection may enable further improvements in pharmacovigilance, drug regulation and recommendation of action for risk minimization.

## References

1. Guideline on good pharmacovigilance practices (GVP) (2011) – Module IX.
2. Ronald Meyboom HB, Antoine Egberts CG, Ralph Edwards I, Yechiel Hekster A, Fred de Koning HP et al. (1997) Principles of signal detection in pharmacovigilance. Drug Safety 16: 355-365.
3. Ola Caster, Kristina Juhlin, Sarah Watson, Niklas Nore´n G (2014) Improved Statistical Signal Detection in Pharmacovigilance by Combining Multiple Strength-of-Evidence Aspects in vigi Rank. Drug Safety (2014) 37:617–628.
4. The importance of pharmacovigilance – safety monitoring of medicinal products. World Health Organization (2002), Geneva.
5. Suzanne Gagnon, Peter Schueler, James Dachao Fan (2012) Global Clinical Trials Playbook.
6. Atusko shibata, Manfred Hauben (2011) Pharmacovigilance Signal Detection and Signal Intelligence Overview.