Guidance for Industry: Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment

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The Role of Pharmacovigilance in Risk Management

Pharmacovigilance **refers to all post-approval scientific and data gathering activities relating to adverse event**

- **detection**
- **assessment**
- **understanding**

This includes the use of pharmacoepidemiologic studies

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The Role of Pharmacovigilance in Risk Management

At the time of approval, clinical trial data are available on limited numbers of patients treated for relatively short periods

After approval, large numbers of patients may be exposed chronically, including patients with co-morbid illnesses and those prescribed multiple concomitant medications

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The Role of Pharmacovigilance in Risk Management

A ***safety signal*** refers to a concern about an apparent excess of adverse events compared to what would be expected

After a safety signal is identified, it should be further assessed (e.g., careful case level review) to determine whether it represents a ***potential safety risk***

Further study may be warranted. The methods best suited to address the particular signal or research question should be chosen.

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Identifying and Describing Safety Signals

Good pharmacovigilance practice starts by acquiring complete data from spontaneous adverse event reports or ***case reports***

Case reports are used to develop ***case series*** to describe patient demographics, dosing information, use of concomitant medications, and presence of co-morbid conditions

For any individual case report, it is rarely possible to know with a high level of certainty whether the event was caused by the product

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Identifying and Describing Safety Signals

Data mining techniques **may be applied to large adverse event databases to identify unusual or unexpected product-adverse event combinations**

Application of these techniques is considered exploratory, given the reporting biases inherent in voluntary adverse event reporting systems

Data mining is not a tool for establishing causal attributions between products and adverse events

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Identifying and Describing Safety Signals

Comparisons of *reporting rates* for adverse events can be valuable, particularly across similar products or across different product classes prescribed for the same indication

Such comparisons are subject to substantial limitations in interpretation given the uncertainties in the numerator and denominator used and should be viewed as exploratory

Reporting rates are not incidence rates

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Investigating a Signal Through Observational Studies

Pharmacoepidemiologic safety studies **are non-randomized observational studies that may be used to characterize safety signals. Unlike case series, they**

- **have protocols and control groups**
- **test pre-specified hypotheses**
- **allow for the estimation of relative risk of an outcome**

Sponsors can initiate pharmacoepidemiologic safety studies at any time

- **at initial marketing to address residual concerns**
- **when a safety signal is identified after approval**

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Investigating a Signal Through Observational Studies

Through the creation of *registries*, a sponsor can follow up on safety signals identified from case reports or other sources and evaluate factors that affect the risk of adverse outcomes

Registries can be useful for collecting data from multiple sources

- **physician records**
- **hospital summaries**
- **pathology reports**

Registries can be initiated at any time

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Investigating a Signal Through Observational Studies

Surveys **of patients or health care providers can gather information to assess**

- **knowledge about labeled adverse events**
- **use of the product (including compliance with *RiskMAP*)**
- **confusion over sound-alike or look-alike trade names**

Surveys can be initiated at any time

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Developing a Pharmacovigilance Plan

For most products, routine pharmacovigilance is sufficient for postmarketing risk assessment

In certain instances, unusual safety risks may suggest the need to consider a *pharmacovigilance plan*

- **describes efforts above and beyond routine spontaneous reporting**
- **enhances or expedites the sponsor's acquisition of safety information**

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Developing a Pharmacovigilance Plan

A sponsor's pharmacovigilance plan may involve

- **expedited reporting of serious adverse events of interest**
- **adverse event summaries at more frequent intervals**
- **additional observational studies or clinical trials**
- **implementation of active surveillance activities**

Pharmacovigilance plans may be developed at any time

Emerging new safety data may result in ongoing revisions to the sponsor's pharmacovigilance plan

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For additional information consult:

www.fda.gov/cder/guidance/6359OCC.htm