

Regulatory Intelligence: Pharmacovigilance

acorn
REGULATORY



**Introduction to Regulatory Intelligence:
Pharmacovigilance
by Dr. Gemma Robinson**

3

Introduction

Contact Acorn Regulatory

4

Contact
Acorn Regulatory

**Good Pharmacovigilance Practice (GvP) &
Social Media**

5

Good PV Practice (GvP)
and Social Media

**PV KPI's: Pharmacovigilance Key Performance
Indicators**

6

PV KPI's:
Pharmacovigilance
Key Performance
Indicators

**Does Your PSUR Process Stand Up To
Scrutiny?**

8

Does Your PSUR Process
Stand Up To Scrutiny?

**Acorn Regulatory
Pharmacovigilance Services**

10

Acorn Regulatory
PV Services

Welcome



Welcome to our first sector specific e-book.

Regulatory Intelligence: Pharmacovigilance highlights just a small amount of the pieces written by our expert staff in recent times. These pieces have appeared in print and online. Some of the pieces featured here are new pieces created specifically for this e-book.

Our pharmacovigilance team works with a wide range of companies around the world. They work on some of the most important and ground breaking treatments available. They have, quite rightly, a well won reputation for excellence amongst their peers and clients.

As always, I welcome any thoughts or comments that you may have on the publication.

**Dr Gemma Robinson,
Managing Director,**

Tel: 00353 52 61 76 706

E-Mail: gemma.robinson@acornregulatory.com

Contact Us

If you would like to talk to us about how we can help you with your pharmacovigilance contact us today.



**Dr Gemma Robinson,
Managing Director,**

Tel: 00353 52 61 76 706

E-Mail: gemma.robinson@acornregulatory.com

**Brian Cleary,
Chief Marketing Officer,**

Tel: 00353 52 61 76 706

E-mail: brian.cleary@acornregulatory.com



Good Pharmacovigilance Practice (GvP) & Social Media

Good Pharmacovigilance Practice (GVP) at its core aims to prevent harm from adverse reactions in humans from medicines and to promote the safe and effective use of medicinal products. Pharmacovigilance professionals are aware that adverse reactions can be reported from a variety of sources – patients, healthcare professionals, competent authorities or marketing authorisation holders. Robust Pharmacovigilance however depends greatly on complete and timely reporting of adverse reactions. And herein lies the problem – it is estimated that over 90% of adverse drug reactions are under-reported ⁽¹⁾.

Is there a solution? Social media and big data have the potential to revolutionize the current approach to Pharmacovigilance. The advent of social media has been transformative in areas such as marketing, breaking news, recruitment and the way we interact with others around the world. And like anything else, people may share their experiences about their medication on such platforms or on patient forums.

Problem solved you might think? Well, not quite.

Current Pharmacovigilance guidance dictates that a valid individual case safety report should include at least one identifiable reporter, one single identifiable patient, at least one suspect adverse reaction and at least one suspect medicinal product. Any or all of these items could be missing from a social media post. Patients or drug identity may be difficult to identify, the description of the adverse reaction or duration may be vague etc.

Social media as a reputable source of information for media outlets faced similar problem in the recent past. Here in Ireland, Dublin based Storyful was one such company that addressed this with their news verification offering.

While the FDA has issued social media guidance documents in 2014, these were focused on advertising and do not provide guidance on pharmacovigilance. There are a number of collaborations on-going between technology service providers and both regulators and big pharma. We expect to see significant movement in area in the years ahead.

Ref 1: Hazell L, Shakir SAW. Under-reporting of adverse drug reactions. Drug Saf. 2006;29:385-396.

PV KPI's: Pharmacovigilance Key Performance Indicators

Key performance indicators (KPI) are a set of quantifiable measures that a company uses to gauge its performance over time. These quantifiable measures can be used to indicate how well a pharmacovigilance system is performing and whether the system is continually improving. The demands on a PV system vary depending on number of products concerned, the nature of the products and the life cycle and regulatory demands placed on the products.

Module I of the GVP Guidance (I.B.12.)– Pharmacovigilance systems and their quality systems require the “Monitoring of the performance and effectiveness of the pharmacovigilance system and its quality system”.

Guidance on compliance monitoring for each pharmacovigilance process is provided in each Module of GVP as appropriate, however measuring compliance with requirements is not the only way to measure the performance of a PV System. Too many MAH's limit the reporting of KPIs to the system's compliance with reporting timelines (e.g. expedited reporting of ICSRs, PSUR submissions and PRAC Variations).

In order to generate an effective evaluation of the PV system that will be of value, the following criteria should be considered:

- Assessments/evaluations should be timely - accounting for time required for the implementation of e.g. a new procedure/intervention/RMP/Variation
 - Evaluation should address all (relevant) aspects of the PV system
 - The evaluation strategy should include outcomes that can be realistically measured that will not generate inaccurate or misleading data
- Key Performance Indicators

Structural Indicators measure systems and physical infrastructures. These indicators provide an assessment of current PV documentation and resource compliance with regulatory PV expectations and requirements.e.g. Existence of Company PV SOPs that reflect current practice, current GVP requirements and as documented in the PSMF Process Indicators measure how the system works. These provide insight into what extent the PV System is being implemented as planned e.g. SOP/SDEA/PSMF compliance.

Implementation metrics are identified in advance and tracked over time as this helps to support and correct implementation where necessary e.g. by re-Training, updating SDEAs, reviewing procedures e.g. Existence of an audited system for coordination and collation of pharmacovigilance data from all sources in the country (e.g., literature, MAH's, EMA, CA's, medical enquiries, complaints).

Outcome Indicators measure final product of the inputs made into PV activities. These provide an overall measure of the level of risk control (patient safety) that has been achieved with the PV system in place.

Examples of these indicators would be;

- number of audit findings,
- number of PRAC requests for safety updates to patient information,
- percentage compliance with safety data reporting timelines.

Key performance indicators should be re-evaluated to assess their relevance as indicators, and targets can be re-set when deemed appropriate. As a consequence of the monitoring of the PV System performance, corrective and preventive measures can be implemented where deemed necessary, resulting in continuous improvements to the PV System.

Does Your PSUR Process Stand Up To Scrutiny?

Periodic safety update reports (PSURs) are pharmacovigilance documents intended to provide a safety update resulting in an evaluation of the impact of the reports on the risk-benefit balance of a medicinal product. They are submitted by marketing authorisation holders (MAHs) at defined time points during the post-authorisation phase. MAHs are required to submit PSURs once a medicinal product is authorised in the EU, regardless of its marketing status.

The legal requirements for submission of PSURs are established in the Regulation (EC) No 726/2004 and the Directive 2001/83/EC. The format of PSURs shall follow the structure described in the Commission implementing Regulation (EU) No 520/2012. The EU PSUR single assessment, referred also as PSUSA, is the assessment of PSURs for medicinal products subject to different marketing authorisations containing the same active substance or the same combination of active substances and for which the frequency and dates of submission of PSURs have been harmonised in the list of EU reference dates (referred also as EURD list).

The Periodic Safety Update Report (PSUR or PSUSA) is often overlooked by MAHs when it comes to Regulatory Pharmacovigilance (PV) Inspection preparation. Once the PSUR has been submitted on time and the assessment report received and acted upon by the MAH, the PSUR is often filed away and “forgotten”. This is an oversight – PSUR production is, more often than not, included in the scope of the PV Inspection as a reliable indicator of PV system performance.

Typical inspection findings relating to PSUR production include; no formal procedures in place for PSUR production, no quality control checks of PSURs, PSURs not containing all of the required information, no non-serious unlisted line listings, inadequate discussion of lack of efficacy, special populations or pregnancy exposure, PSURs submitted late to competent authorities or not at all, failure to fully address Assessment Report comments, not including follow-up reports and inadequate evaluation & discussion of issues of concern.

Inspectors could use the PSUR procedure as a key PV system performance indicator in any or all the following ways:

The PSUR process maintained by the MAH can demonstrate to the Inspectors:

- MAH compliance with legislation (submission timelines, PSUR content etc.)
- MAH compliance with their own procedures
- MAH compliance across departments (medical affairs, regulatory affairs and PV)

Evidence of good documentation practice (decisions and actions taken, QC review)

MAH QPPV oversight and governance – awareness of the safety profile of the product, actions taken to address issues and clear communications between departments

What the PSUR process should be able to demonstrate is that the MAH has in place:

Effective Signal Management
Robust Decision Making
Good Documentation Practice
Effective cross functional decision making (e.g. Regulatory Affairs informed of recommendations made during PSUR compilation)
Efficient PV Processes
QPPV Oversight

Inadequacies in the PSUR production process could signify any or all of the following to the Inspectors: poor communication, incomplete data review or data QC review, poor documentation management and lack of QPPV oversight.

As Inspectors will employ a variety of inspection techniques (interviews, review of procedures and sampling of evidence), it would be wise for the MAH to take the following measures to prevent inspection findings concerning the PSUR process:

- Prepare any/all parties involved in PSUR production for interview.
- Ensure procedures are in place governing each step of PSUR production (data retrieval, data reconciliation, PSUR writing, QC review, medical review and approval)
- Confirm validated search strategies are in place.
- Ensure all parties involved in the PSUR production have been adequately trained and have training records available.
- Where applicable, ensure detailed Work Instructions are in place

Retain evidence to demonstrate:

- Training in PSUR Production (e.g. Training Slides)
- QPPV Oversight (Review and Sign off)
- Minutes of Meetings (All cross functional meetings should be documented)
- PSUR Submission (e.g. Trackers - Evidence of compliance)
- QC Review (Data Checksheets)
- PSUR Audits (Is PSUR production covered in PV audit schedule?)
- Data Outputs (Case Listings & Tables, Signals, Exposure Data, clinical trials)
- Quality Metrics & KPIs (include PSUR production)

It is a sensible approach for MAHs to use their PSURs as starting point when preparing for an inspection or making an assessment of the performance of their PV system. The PSUR evaluates the risk-benefit of the medicinal product, and so ultimately it is the report which relies on safety data sources from a variety of MAH PV processes. Deficiencies in any of these procedures will lead to a deficient PSUR. PV Inspectors are wise in interrogating the PSUR process during a PV inspection.

Pharmacovigilance Services

Acorn Regulatory Pharmacovigilance Services

We work with companies around the world every day. Right now, we are working as a 'virtual pharmacovigilance office' for many of the most dynamic healthcare manufacturers in the world. They trust us to act on their behalf because of our long-held reputation and our commitment to service excellence.

The legal requirement for a quality assured pharmacovigilance system was introduced with the publication of the new Pharmacovigilance legislation 'Directive 2010/84/EU'. Acorn Regulatory's pharmacovigilance team have worked tirelessly in developing a pharmacovigilance system that is adequate and effective in conducting the specific pharmacovigilance processes required to fulfil the tasks and responsibilities outlined in the current legislation.

We have worked with many SME Pharmaceutical manufacturers over the years. In particular, we have been representing companies as their virtual pharmacovigilance office. Our role is to ensure that you can continue to market your medicines in a safe and effective manner. By regular communication with our clients, we also ensure that we are involved in any third party negotiations which may have an impact on pharmacovigilance. The addition of a new product may require new safety data exchange agreements or revisions to existing agreements. We have our own customised templates to suit almost every situation.

If you would like further details about our pharmacovigilance services contact us:

**Acorn Regulatory,
Suite 6 Powerstown House,
Gurtnafleur Business Park,
Clonmel,
Co. Tipperary,
E91 V9P7.**

**Tel: 00353 52 61 76 706
Email: info@acornregulatory.com**

Our Expert PV Team

Acorn Regulatory Pharmacovigilance Services



**Vanessa Hyde,
Senior Regulatory Affairs Advisor**



**John McIntyre,
Senior Regulatory Affairs Advisor**



**Gemma Robinson,
Managing Director**



**Eileen Shortiss,
Senior Regulatory Affairs Advisor**



acorn

REGULATORY

**Acorn Regulatory,
Suite 6 Powerstown House,
Gurtnafleur Business Park,
Clonmel,
Co. Tipperary,
E91 V9P7.**

Tel: 00353 52 61 76 706

E-mail: info@acornregulatory.com

Web: www.acornregulatory.com