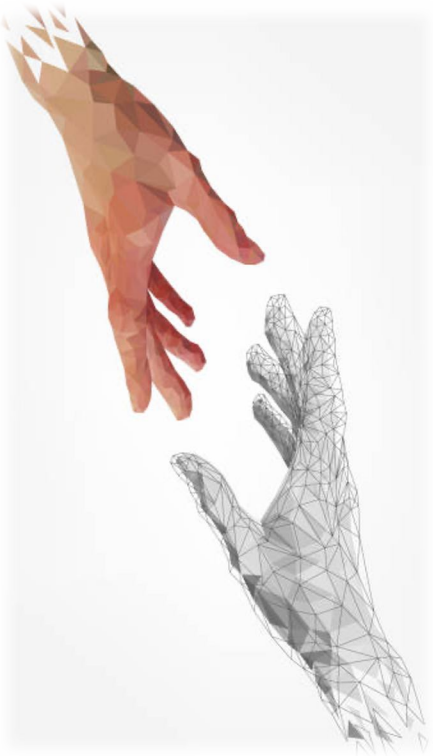
RED LINE Pharmacovigilance

Pharmacovigilance Outsourcing Partner

Risk management services for the pharmaceutical industry.

RED LINE

PHARMACOVIGILANCE



"A good relationship with the MAH is critical."

Good pharmacovigilance practice is dependent on a sound understanding of the key principles of this science.

Legislation is global and the process is complex.

Red Line Pharmacovigilance Ltd is a small, emerging company established in 2010.

Our Managing Director, Shirley-Ann van der Spuy is a qualified pharmacist with a post-graduate qualification in pharmacovigilance and over 20 years experience in the pharmaceutical industry. Her portfolio is broad and her experience extends to many facets in the world of pharmacy, which includes community pharmacy, quality control, regulatory affairs, medical information and pharmacovigilance.

Our Technical Director, Ben van der Spuy has many years experience in project management and spent 12 years working for Accenture Services, managing large software development teams and budgets of tens of millions of pounds.

As co-owners and company directors, we believe in the philosophy of '*learning to walk before you run*.' Our primary focus has been to build a strong foundation, the backbone of which is the provision of a quality service. We have purposefully managed a slow expansion process to ensure service levels are maintained and staff are not overstretched.

Our team has been carefully and meticulously selected. All staff have a strong background in the healthcare industry and a sound understanding of life sciences.

Our mission statement:

"One cannot change whether a drug causes an adverse reaction. What can be changed is whether a manufacturer did everything possible to detect it.' - *Strom BL, Pharmacoepidemiology, 4th Edition. 2005.*

A range of scientific services tailored to cover human pharmaceuticals and medical devices.

We do business with clients who want to do things right.

"It takes many good deeds to build a good reputation and only one bad one to lose it."
– Benjamin Franklin

At Red Line our focus is on maintaining our reputation of honesty and integrity. We are a company who don't compromise on quality. At the same time, we are committed to providing a cost-effective service to our clients.

We understand the monetary investment required for product development and commercialisation. We believe cost effective prices assist in promoting better compliance. If costs are not excessive the client can be confident their budget meets the needs for regulatory compliance and can better manage the costs associated with a medicinal compound.

Healthcare starts with pharmaceuticals, their research, testing and continued development to ultimately produce a quality medicinal product. These advances save or extend the lives of patients, ease the cost of healthcare for government bodies and change the outcome of many future generations. Red Line takes great pride in walking this path with its clients and ensuring the therapeutic goals of the medicinal product are always kept in focus.

We believe in forming strong collaborative relationships with our partners and provide a range of services to support the pharmacovigilance process. Our team is proficient in adverse event case processing, literature monitoring, causality assessment and medical review.

We can manage your registration with Eudravigilance and conduct electronic reporting to regulatory authorities on your behalf. For smaller companies this function can be extended to include the management of the medicinal product dictionary (xEVMPD) portal.

Backend pharmacovigilance services extend to the writing of standard operating procedures, clinical dossiers, medical writing, risk management plans, periodic safety update reports, clinical expert statements and the compilation of reference safety documentation, such as company core data sheets, summary of product characteristics and patient information leaflets.

Complimentary services include medical information enquiry handling and copy approval. We have invested in a bespoke IT solution, a medical enquiry tracking system (METS), which provides a full history and audit trail of the medical enquiry handling process and reconciliation with linked departments.

Copy approval can be performed for any promotional materials to ensure compliance with the ABPI code and appropriate legal requirements. Where signatory resources are stretched we can provide final medical and non-medical signatory support.

Safety monitoring

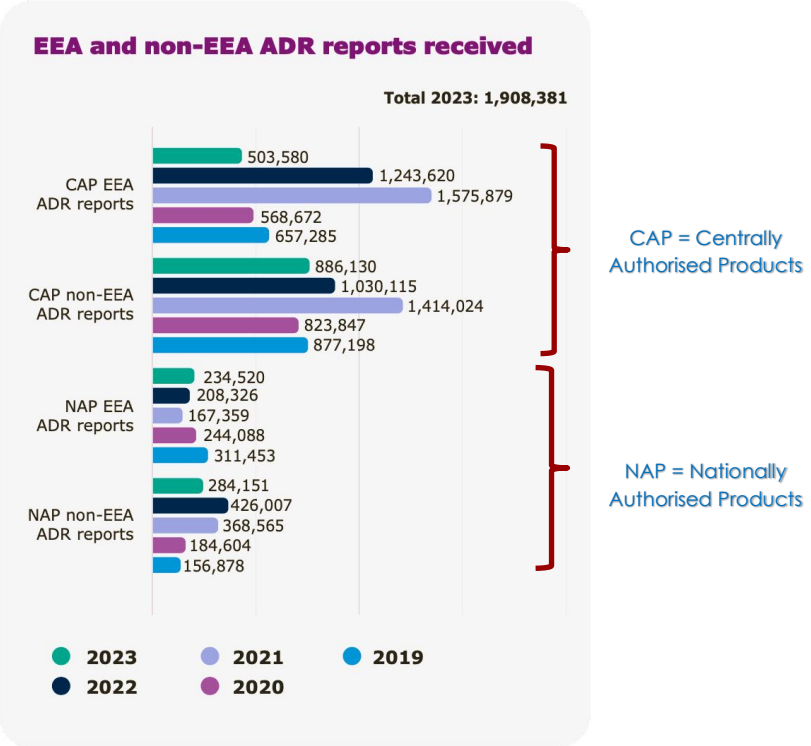
Once the medicine is authorised, EMA and national authorities continuously monitor its safety.

Pharmacovigilance is a discipline that has been around since the early 1960's and although it is still a young science, pharmacovigilance has undergone many changes over the last two decades. The principle change is that of risk management whereby companies continuously ensure the benefits of a medicinal product always outweighs any potential risk to the patient.

Since the thalidomide tragedy in the 1960's, which resulted in the disfigurement of thousands of children, drug safety has become a global concern. Worldwide regulatory authorities have collaborated to produce international guidance (ICH guidelines) to provide a framework for this discipline for the pre and post marketing phases of drug development.

Annual Report on ADR reports from the European Medicines Agency (2023)

Over 1.9 million ADR reports were submitted to Eudravigilance in 2023, representing a substantial decrease of 34% compared with 2022. Over 60% of all reports originated outside the EEA.



The higher reporting rates, including patient reporting, during the COVID pandemic were as a result of the mass vaccination campaigns and the heightened awareness of the importance of reporting suspected side effects.

The reports submitted by European patients and consumers also decreased in 2023 when compared to reporting rates in 2021 and 2022 and are more in line with reporting rates during pre-pandemic years.

Annual Report on pharmacovigilance activities from the European Medicines Agency (2023)

Signal Detection

A safety signal is information on a new or known adverse event that is potentially caused by a medicinal product and requires further investigation. Signals arise from various sources, such as spontaneous adverse event reports from the market, clinical studies, and scientific publications. Safety signals are investigated to determine whether a causal relationship exists between the adverse event and the medicine.

In 2023, the EMA reviewed 1,364 potential safety signals. Of these, 74% originated directly from the Eudravigilance database. The PRAC committee assessed 71 signals, of which 39 were confirmed as new safety concerns requiring further action.

Periodic Safety Update Reports (PSURs)

Marketing Authorisation Holders are required to submit reports to regulatory authorities at regular intervals in order to evaluate a medicines benefit-risk balance. These reports are called PSURs, and the assessment procedure is referred to as a 'periodic safety update single assessment' or PSUSA.

In 2023, PRAC assessed 859 PSURs, of which 28% were related to NAPs. The outcome of the assessment of these PSURs resulted in changes being made to 15% of products for which reports were submitted. The changes impacted the product information (SmPC and PILs) resulting in wording updates to optimize the safe and effective use of these medicines by patients and healthcare professionals.

Outcome of signal assessment

1,364 potential signals reviewed by EMA

71 confirmed signals were prioritised and assessed by the PRAC

- Of these 71 signals, 39 were detected and validated by EMA;
- 32 were detected and validated by EU Member States.

Out of 71 confirmed signals

- 19 signals led to a product information update;
- 13 signals led to a recommendation for routine pharmacovigilance; and
- 39 signals were undergoing review by the PRAC at the end of 2022 as further data were required.

Responsibility for Pharmacovigilance

Marketing Authorisation Holder. (MAH)

The marketing authorisation holder is responsible for the pharmacovigilance tasks and responsibilities as laid down by local regulations and **assumes full responsibility and liability** for its authorised medicinal products to ensure that appropriate actions can be taken when necessary. The MAH must **establish pharmacovigilance system and appoint a QPPV** who is permanently and continuously at their disposal. The MAH must register the details of the QPPV to local regulatory agencies. The MAH must **ensure the QPPV have sufficient authority** to be able to influence and affect change to the pharmacovigilance and quality systems and is notified of any changes made to it, including contractual obligations with third parties.

Qualified Person for Pharmacovigilance. (QPPV)

The appointment of a QPPV is a UK and EU legal requirement. This person is responsibilities for the establishment and maintenance of the MAH's pharmacovigilance system and must have sufficient **authority over the pharmacovigilance and quality systems** to act in full compliance of the laws of that country. The QPPV assumes the lead role in pharmacovigilance services and activities, the aim of which is to ensure that every medicinal product has the best possible safety profile. The QPPV acts as a single point of **contact for regulatory authorities** and is expected to be available on a 24-hour basis. The QPPV can act on behalf of more than one MAH. A **deputy QPPV is required** to provide back up support to the QPPV in times of absence.

National Responsible Person. (NCP)

Although companies may appoint a QPPV, certain countries (including the UK) require the appointment of a **National Contact Person (NCP) or Local Responsible Person (LRP)** for pharmacovigilance. This person must reside in the respective country and **reports directly to the QPPV**. The details of the NCP must be registered with the local regulatory agency. This individual must be able to **facilitate responses to pharmacovigilance queries** raised by the **regulator in the local language**. In the UK, the NCP must have access to the UK Pharmacovigilance System Master File and be provided access to UK safety reports held on the global safety database. An appointed back up person or deputy is not required for this role for absences of <1 month.

Pharmacovigilance.

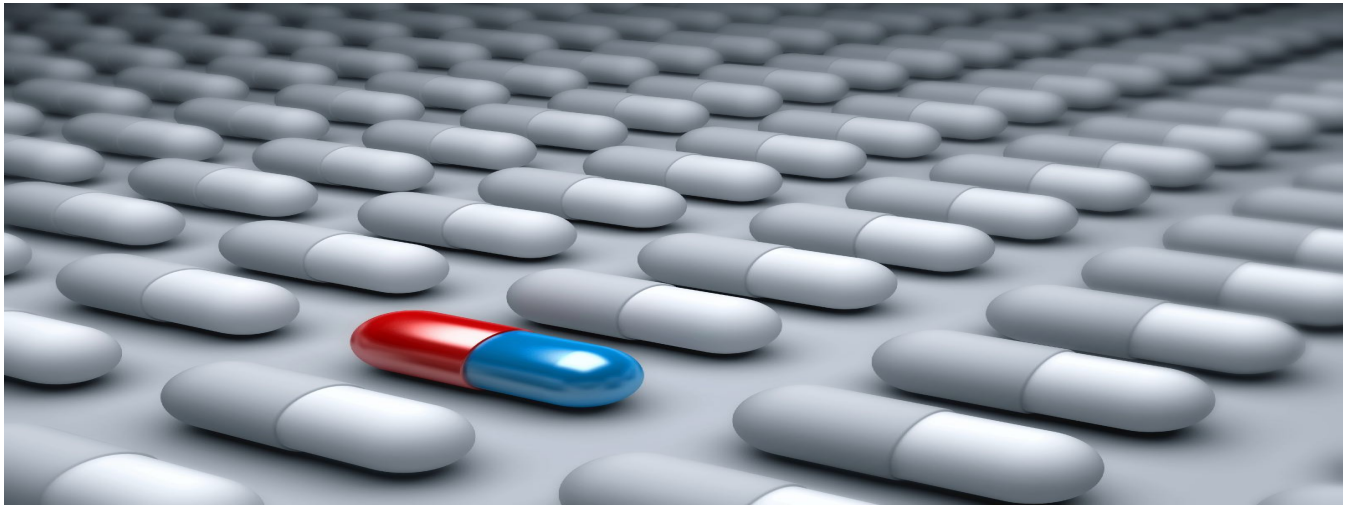
Individual Case Safety Reports (ICSRs) require a thorough review by the MAH. Each case must pass through a **pre-screening triage** to assign 'report-ability' and associated deadlines. Cases must undergo assignment of **MedDRA terms** to prepare for expediting. Each report undergoes **causality** assessment, **narrative** writing and a final **review by a medically qualified member of staff**. This process underpins the fundamental pharmacovigilance system and **getting it right from the start is paramount** to ensuring aggregate reports produced from the data generated is reflective of the true benefits and risks of the product. The electronic reporting of all adverse events is a mandatory requirement throughout the European Union.

Medical Information.

We provide complementary services to clients enabling a seamless transition between **medical information**, product **quality complaint handling** and **adverse event follow up** and investigation. Medical information and pharmacovigilance teams should **work collaboratively** at all times. Representing the '*face of the firm*' staff members should be knowledgeable about company products and the **scientific service** they provide to healthcare professionals, members of the public and internal staff is valued. At Red Line we ensure our medical information team have past experience in the healthcare industry and a good grounding in life science. **High standards** and **quality patient care** is always our top priority.

Risk Management.

The focus of pharmacovigilance has shifted towards risk management. New applications for marketing authorisations require the submission of a risk management plan. In addition to the requirement for companies to have a system in place to collect and report adverse events, they are expected to **monitor trends** with this data to enable a continued assessment of the **risk-benefit profile** during the entire life-cycle of the product. Companies are expected to act on **emerging safety information** or changes in the safety profile that negatively impact the end user. These changes are reflected in key **reference safety documents**, the Summary of Product Characteristics (SPC) and the Patient Information Leaflet (PIL). Pharmacovigilance impacts regulatory departments, marketing, sales and legal teams.



RED LINE Pharmacovigilance Ltd

Suite 2.12, Challenge House, Sherwood Drive, Bletchley
Milton Keynes, MK3 6DP, United Kingdom

Tel: +44(0)330 1359 436 Email: info@redlinepv.co.uk

www.redlinepv.co.uk

August 2024

RED LINE
PHARMACOVIGILANCE