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Navigating Local Pharmacovigilance in European Countries, UK and Switzerland

ASPHALION
Knowledge from experience

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1. Introduction

Local pharmacovigilance (PV) requirements in European countries are a complex process due to the diverse regulatory landscape. To ensure compliance with local safety requirements, it is essential to understand both the overarching European Union (EU) regulations and the specific national requirements that may vary from one country to another.

In Europe, pharmacovigilance activities governance, falls under the jurisdiction of the European Medicines Agency (EMA) in accordance with EU Pharmacovigilance Legislation (Regulation (EU) No 1235/2010).

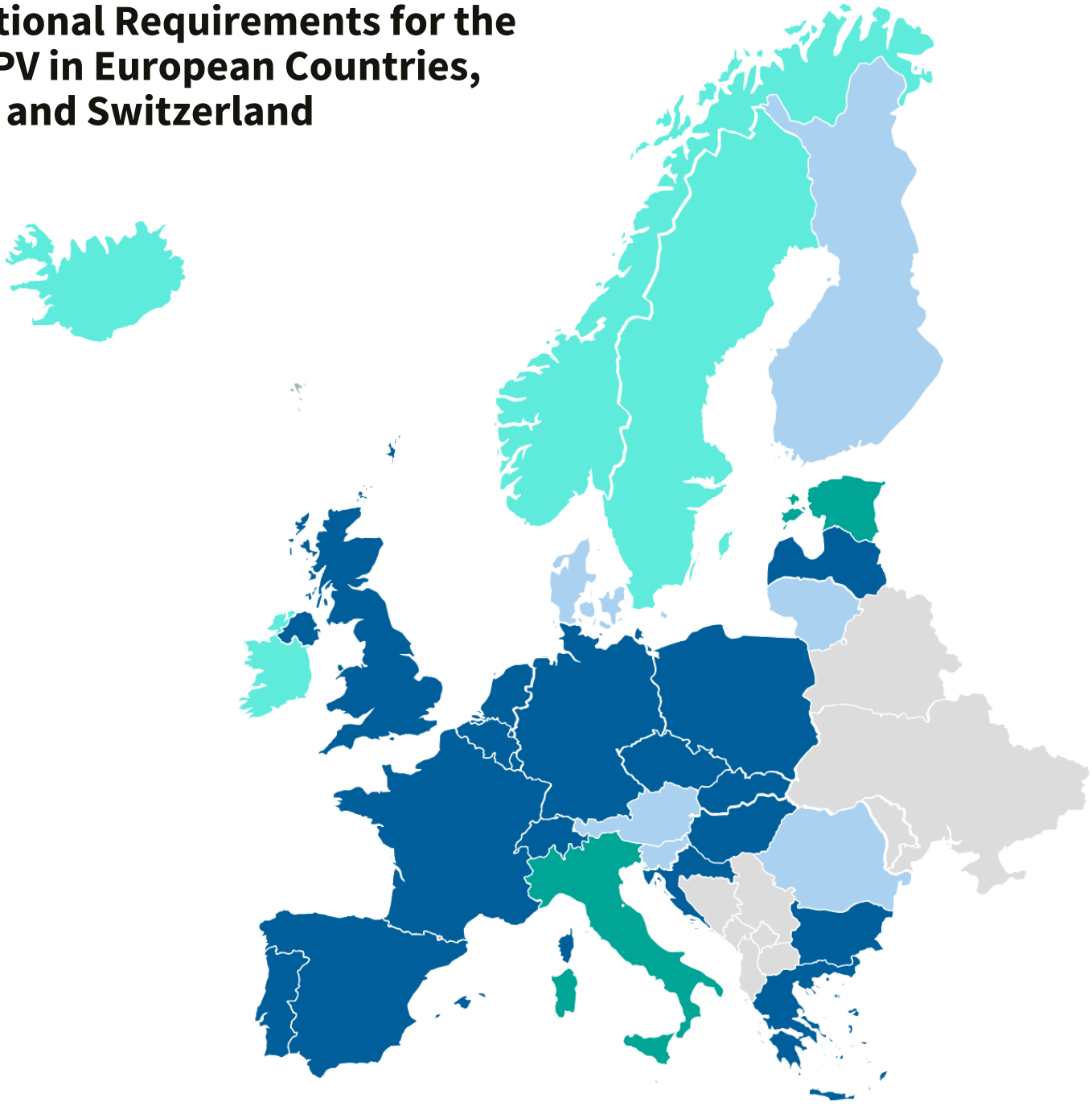
Nonetheless, when it comes to the application and enforcement of these rules, variations may arise at the national level. These differences may be evident in a range of key activities, including the need of appointing a local pharmacovigilance contact, local literature searches, local regulatory intelligence and other activities such as risk minimization activities linked to the Risk Management Plan (RMP) with each country having its own specific requirements.

MAHs need to be aware of both the individual national requirements and the overarching EU regulations. These national discrepancies present a complex landscape for pharmaceutical entities operating across different EU countries, as they must ensure adherence to each nation's specific pharmacovigilance requirements.

Specifically, MAHs often encounter challenges in determining in which countries they must have a local pharmacovigilance contact. A local pharmacovigilance contact, also known as a local pharmacovigilance representative, is an individual or an organization appointed within a country to perform pharmacovigilance-related duties. This role typically includes being available for authorities 24/7, maintaining local PV systems, and ensuring compliance with the local regulatory requirements.

In this guide, Asphalion provides you with a country-by-country visual summary of the requirements that as an MAH must be considered when marketing medicinal products in various European countries, as well as in the UK and Switzerland.

National Requirements for the LPPV in European Countries, UK and Switzerland



REQUIRED

Belgium
Bulgaria
Croatia
Cyprus
Czech Republic
France
Germany
Greece
Hungary
Latvia
Luxembourg
Nehterlands
Poland
Portugal
Slovakia
Spain
United Kingdom
Switzerland

MAY BE REQUIRED

Austria
Denmark
Finland
Lithuania
Malta
Slovenia
Romania

IN CERTAIN CIRCUMSTANCES

Estonia
Italy

NOT REQUIRED

Iceland
Ireland
Norway
Sweden

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2. 2. 1. Requisites per country

EU COUNTRIES WHERE HAVING A LCCPV IS REQUIRED

CROATIA 	
Croatian Agency for Medicinal Products and Medical Devices (HALMED)'s requirements are some of the **strictest in Europe**	
Education	Medical Doctor (MD) specialized in clinical pharmacology, or a doctor of dental medicine*, or a pharmacist*, or a master of medical biochemistry*, or a doctor of veterinary medicine *If the person responsible for PV is not a Medical doctor, access to a Medical doctor must be available and appropriately documented.
Experience	At least 2 years of experience in PV or 2 years of experience in his/her profession.
Training	Documented training in (1) in PV terminology, (2) spontaneous and solicited reporting of adverse reactions (ADRs), and (3) methods of ADR reporting, evaluation of ADRs, preparation of Individual Case Safety Reports (ICSRs), PSURs, RMPs, and DSURs.
Deputy	Needed
Other considerations	MAH appoints one LPPV for each PV system regarding medicinal products that have marketing authorization in the Republic of Croatia
Local legislation	Ordinance on Pharmacovigilance (Official Gazette 83/13) p.7 Ordinance on Pharmacovigilance (Official Gazette 83/13) Article 32 Medicinal Product Act (official gazette no. 76/13) Article 3 Point 58

GREECE 	
The Greek national competent authority (EOF) has stated that the LPPV in Greece **is appointed by the EU QPPV for human medicinal products**	
Education	Have a degree in medicine, dentistry, biology, biochemistry, chemistry, veterinary medicine, or nursing highest (Higher Education).
Experience	2 years of experience in pharmacovigilance.
Other considerations	-This person should also have an excellent knowledge of English -Not belonging nor related to the marketing or promotion departments -The LPPV is responsible independently and in parallel with the MAH
Local legislation	Ministerial Decree no. Δ.ΥΓ3α/Γ.Π. 32221 ΦΕΚ 1049/29-04-2013

FRANCE	
Education	Be a Medical Doctor (MD) or a Pharmacist
Experience	Have experience in PV
Timing	The appointment of an LPPV must be made as soon as a company uses a medicine.
Deputy	There is no requirement to have a deputy (here is no obligation to communicate to the ANSM the name of the deputy LPPV in the event of absence.) but it is necessary to provide a documented backup system for the LCPPV in the event of its absence.
Other considerations	For France, it is important to make the difference between the LCPPV and Responsible Pharmacist (Pharmacien Responsible, PR). They can be one and the same person, but they are not the same role.
Local legislation	Code de la Santé Publique, article R.5121-164

THE NETHERLANDS	
Education	Be medically qualified or have access to a medically qualified person (such access must be appropriately documented)
Experience	Adequate qualifications on PV (experience and training)
Timing	She/he should be appointed at the moment that a MAH will market a product in the Netherland
Local legislation	Not specified in the Dutch legislation, but Dutch regulatory authorities have outlined a general guidance for such a person.

HUNGARY	
LCPPV in Hungary is **only needed if the EU QPPPV is outside Hungary**	
Timing	The appointment in Hungary must be done with the launch of the product to the Hungarian market
Deputy	The decree does not establish the requirement of having a deputy. This is determined by the MAH
Other considerations	The Decree does not establish the requirement of 24h availability . This is determined by the MAH
Local legislation	Hungarian Decree 15/2012 (VIII. 22.) of the Ministry of Human Resources on the Pharmacovigilance of Medicinal Products for Human Use

GERMANY	
Also called “Stufenplanbeauftragter” / Graduated Plan Officer	
Education, experience and training	The requirements for the LCPPV in Germany (the “Stufenplanbeauftragter” / Graduated Plan Officer) are equal to those of the EU QPPV.
Deputy	In addition to the “Stufenplanbeauftragter,” a Deputy with equal qualifications is required
Other considerations	There is no requirement for the Graduated Plan Officer to speak German or be a resident of Germany; theoretically, he/she can be a resident of any Member State of the European Union. However, the “Stufenplanbeauftragter” has to communicate with the BfArM and the competent authorities in the federal states (Landesbehoerden), and this communication is done almost exclusively in the German language; therefore, it is almost impossible for the Graduated Plan Officer to fulfill his role without being able to speak German.
Local legislation	§63a of the German Drug Law (AMG)

CZECH REPUBLIC AND SLOVAKIA	
The same person can act as LCCP for both	
Education and training	**Slovakia:** Have good knowledge and skills of pharmacovigilance issues.
Other considerations	**Slovakia:** -Be able to communicate in Slovak or Czech language. -This person can be out of Slovakia, but pharmacovigilance activities have to be applied in Slovakia. **Czech republic:** -Be able to communicate in Czech or Slovak language. -Be contactable on the phone number with the Czech country calling code.
Local legislation	**Slovakia:** law on medicines and medical devices 362/2011, §68, art.14 **Czech Republic:** Act on pharmaceuticals, section 91a (3)

CYPRUS AND POLAND	
Education	Be a qualified healthcare professionals or a biologist or a chemist
Training	Having received appropriate training in PV
Local legislation	**Cyprus:** The Drugs for Human Use (Quality Control, Supply and Prices) Law of 2001 (70 (I) / 2001) **Poland:** Announcement president of the medical products registration office, medical devices and biocidal products of august 1, 2024.

BELGIUM, PORTUGAL, SPAIN, LUXEMBURG, BULGARIA & LATVIA	
Local requirements for these countries are quite similar	
Experience and training	Adequate qualifications on PV (experience and training)
Other considerations	**Portugal:** - In Portugal the nomination is within the submission of the MA dossier **Luxemburg:** - Knowledge of French, German English or Luxembourgish to communicate with national stakeholders **Latvia:** - LCPPV is mandatory unless the EU QPPV resides and works in Latvia
Local legislation	**Belgium:** Article 66§2 of the Royal Decree 14/12/2006 **Portugal:** National Legislation, Decree-Law n.o 176/2006, 30 August, article n.o 170, number 5 **Spain:** National legislation, article 14 of Royal Decree 577/2013 of 26 July **Luxemburg:** Article 45.-3 of the Grand-Ducal Regulation, amended on December 15, 1992 **Bulgaria:** Law for medicinal products in human medicine, Article 191. (amend. – SG, 102/2012, in force from 21.12.2012) **Latvia:** Regulation No 47, Procedure for pharmacovigilance

OTHER NON-EU COUNTRIES WHERE HAVING A LCCPV IS REQUIRED: UK & SWITZERLAND

SWITZERLAND	
LCPPV	**MAHs are required to designate a LCPPV** who will be responsible for fulfilling the reporting requirements related to ADRs. The MAHs must **inform the Swissmedic of the name and address** of the LCPPV upon request.
24 hour availability	The LCPPV or a deputy must be contactable at least during business hours on Swiss working days. Outside these times, it is recommended that the MAH organizes an on-call service to ensure that a suitably qualified person is reachable at all times in emergencies.
Residence	LCPPV does not need to reside in Switzerland.
Education & Experience	She/he must have extensive knowledge of PV and should be able to provide relevant documentation/certificates on request and must maintain his/her knowledge through continuous professional development.
Other considerations	• This person does not necessarily have to be employed by MAH but his/her responsabilities should be set out in writing. • Switzerland has three official languages (German, French, and Italian), and submissions to Swissmedic may need to be provided in the official language appropriate for the region.

UNITED KINGDOM	
UK QPPV	The MAH in the UK, whether covering the whole of the UK or just NI or GB, must have **permanently and continuously** at its disposal an **UK QPPV operating and resident in the UK or the EU/EEA.** * *When the QPPV is not based in the UK, a national contact person (NCP) for PV must be appointed who is based in the UK and reports to the QPPV.* Once the NCP for PV has been appointed, their details should be notified to the MHRA via the MHRA Submissions Portal.
Education & Training	The QPPV appointed by the MAH must be appropriately qualified, have knowledge of EU/ UK PV requirements and experience in PV (**similar to the EU QPPV**).
Deputy	There is **no requirement to appoint a deputy** for the UK NCP for PV , but **for periods of extended absence greater than one month** (such as maternity leave, long-term sick leave, etc.), it is expected that another individual is assigned as the NCP for PV and their details should be notified to the MHRA within two weeks of the change.
Local legislation	• The UK QPPV´s requirements, roles and responsabilities shall be very similar to that of the EU QPPV. • To establish and maintain a **PV system** for UK authorised products. • **UK PSMF**: The UK PSMF must describe the Global PV system and reflect the global availability of safety information for UK authorised products. **All PSMFs that cover UK authorised products should be registered with the MHRA (UK PSMF number).** • **The UK QPPV should have access to the reports of suspected adverse reactions and the PSMF for UK authorized products.** The individual should be able to facilitate **responses to PV queries raised by the MHRA**, including via inspections.

EU COUNTRIES WHERE HAVING A LCCPV MAY BE REQUIRED

AUSTRIA	
• There are no specific requirements for the local PV person in Austria that would be established by local laws. However, the majority of MAH in Austria generally choose to appoint a LPPV on a **voluntary basis**. • **This is highly unlikely to be requested**.	
Local legislation	Local law (§ 75i (6) AMG)

DENMARK	
• The Danish Health and Medicines Authority reserves the right to request the MAH to appoint a representative in Denmark to acton behalf of the LPPV but no MAH has yet been asked to appoint a contact person in Denmark	
Local legislation	National legislation (Medicines Act § 53), the Danish Health and Medicines Authority (DHMA)

FINLAND	
• The Finnish Medicines Authority (FIMEA) has the authority to request the appointment of a LCPPV. • **If the MAH does not nominate a LPPV, all communications related to ICSRs will be forwarded to the EU QPPV.**	
Education & Training	The LPPV does not need to have a specific medical degree, but it would be beneficial to have knowledge of PV and Regulatory obligations.
Local legislation	National legislation (Medicines Act 30 c §)

EU COUNTRIES WHERE HAVING A LCCPV MAY BE REQUIRED

MALTA	
• There are no specific requirements for the local PV person in Malta • It is not mandatory to appoint a LPPV as long as the EU QPPV is based in the EEA • Unless specifically requested, it is the prerogative of each company to decide on the nomination of a person for PV	
Education	If such a contact person is requested, this person may or may not be medically qualified.
Local legislation	Guidance Notes for Pharmaceutical Companies on Pharmacovigilance Obligations for Medicinal Products for Human Use.

SLOVENIA	

• It is optional, not mandatory.
• The NCA (JAZMP) reserves the right to require a LPPV in individual cases.
• **When it is requested, the LPPV must:**
  ◦ Education: Have a degree in medicine, pharmacy or veterinary medicine or equivalent.
  ◦ Others: Be based in Slovenia or a company established in the country.	

Local legislation	The Medicinal Products Act, Article 133.

LITHUANIA and ROMANIA	
• The NCAs could request the nomination of a LCPPV but this is highly unlikely to be requested. • There are no specific requirements for the local PV person in Lithuania.	
Local legislation	**Lithuania:** Local Law on Pharmacy the State Medicines Control Agency (SMCA). **Romania:** National legislation (*Law 95/2006 with subsequent amendments, art.815 alin.5*).

EU COUNTRIES IN WHICH THE DESIGNATION OF A LCPPV IS REQUIRED IN CERTAIN CIRCUMSTANCES

ESTONIA

- By default, a LCPPV is **not required**.
- An Estonian speaking LPPV is required in cases where prescribers of medicinal products need to be informed about the **safety risks associated to the products**. This includes direct communication to HCPs (DHPC) and materials related to **additional risk minimization measures** in Estonia.

Local legislation	Minister of Social Affairs no. 26 (§ 4 section 4).

ITALY

- **No mandatory** requirement to appoint a LPPV in Italy but it is mandatory for the EUQPPV or LCPPV **to register with the National PV Database, which contains all information in Italian**. So, in practice, if the EU QPPV does not speak Italian,it will be necessary to appoint a LPPV.

Local legislation	AIFA

EU COUNTRIES IN WHICH THE DESIGNATION OF A LCPPV IS NOT REQUIRED

ICELAND, IRELAND, NORWAY & SWEDEN

- **The designation of LPPV in these countries is not required and the presence of an EU QPPV based in the EEA region is considered satisfactory.**

2.2. Local literature searches

To ensure patient safety, companies holding Marketing Authorizations within the EU are tasked with the diligent monitoring of medical and scientific literature. This is a critical step in reporting potential adverse reactions for their approved drugs.

The review process involves a detailed examination of global medical databases and local publications within the countries where the drug is marketed. The goal is to capture a complete picture of the drug's safety profile, including both the benefits and risks, and to stay alert to any new safety concerns that may arise.

How to select appropriate local magazines.
Selecting the appropriate journals for local literature searches in pharmacovigilance involves a few strategic steps. Here's a guide to help throughout the process:

1. **Identifying Relevant Medical Fields**: Begin by determining the medical specialties that are most relevant to your medicinal product. For instance, if your product is related to cardiology, focus on journals that publish research in that field.
2. **Researching Local Impact**: Look for journals that have a significant impact on the local medical community. You can consult with local healthcare professionals or academic institutions to understand which journals are commonly referenced.
3. **Language Considerations**: Ensure that the journals you select publish articles in the local language, making the data accessible to local healthcare providers.
4. **Regulatory Requirements**: Check for any specific guidelines provided by the local health authorities regarding pharmacovigilance literature searches, as some regions may have a list of recommended or required journals.
5. **Access and Indexing**: Choose journals that are indexed in major databases to ensure ease of access and searchability. However, also consider non-indexed journals if they are influential in the local medical community.
6. **Review Frequency:** Opt for journals that have a regular publication frequency to ensure a steady stream of up-to-date information.
7. **Quality and Peer Review**: Prioritize peer-reviewed journals that maintain high standards of scientific rigor and quality.

By considering these factors, you can create a targeted and effective strategy for local literature searches in pharmacovigilance to support the safety monitoring of your product.

When should I start performing local literature searches?
In Europe, the initiation of local literature searches for pharmacovigilance purposes is aligned with the submission of a marketing authorisation application. According to the EU specific requirements, as indicated in VI.C.2.2.3, marketing authorization holders are required to review the global experience with the medicinal product from the time of application submission until the marketing authorisation is granted. This includes scrutinizing published medical literature for any information that could impact the risk-benefit assessment of the product under evaluation.

Even before a product is marketed, literature searches are essential for the preparation of periodic safety update reports and for the notification of emerging safety issues, as outlined in GVP Modules VII and IX.
These searches are mandatory for all products with a marketing authorisation, regardless of their commercial status.

Therefore, **it is expected that literature searching should commence upon the submission of the marketing authorisation application and be maintained consistently while the authorisation remains active**. This ensures that any new information relevant to the safety profile of the product is captured and assessed in a timely manner.

Is there any country with specific requisites?

As for specific country requirements within Europe, while the European Medicines Agency (EMA) provides overarching guidelines for pharmacovigilance practices, individual EU member states may have additional requirements or guidance for conducting literature searches. These local requirements are typically in place to ensure that any safety information specific to the country's population or medical practice is identified and assessed.

For instance, some countries may:

- Require searches in specific local or national medical journals that are not indexed in the major international databases.
- Have particular timelines for how frequently literature searches need to be conducted.
- Mandate that the literature search includes local languages.
- Provide a list of local journals that should be monitored.

COUNTRY SPECIFIC EXAMPLES:

Germany: Often requires pharmacovigilance literature searches to include German-language journals and databases, and there is an expectation to monitor local literature not just for marketed products but also for those in the clinical trial phase.

France: The French National Agency for Medicines and Health Products Safety (ANSM) may have additional requirements for monitoring local literature, particularly in the French language, and sometimes has specific journals that are considered key sources.

Italy: The Italian Medicines Agency (AIFA) may require additional monitoring of Italian-language publications and may have a list of national journals that are considered important for ongoing pharmacovigilance activities.

It's critical for Marketing Authorisation Holders (MAHs) to consult the national competent authorities in each EU member state where their product is authorized to ensure they meet all local pharmacovigilance requirements, including literature searches. This may involve reviewing national guidelines, engaging with local experts, or working with regulatory consultants who specialize in the pharmacovigilance regulations of specific countries.

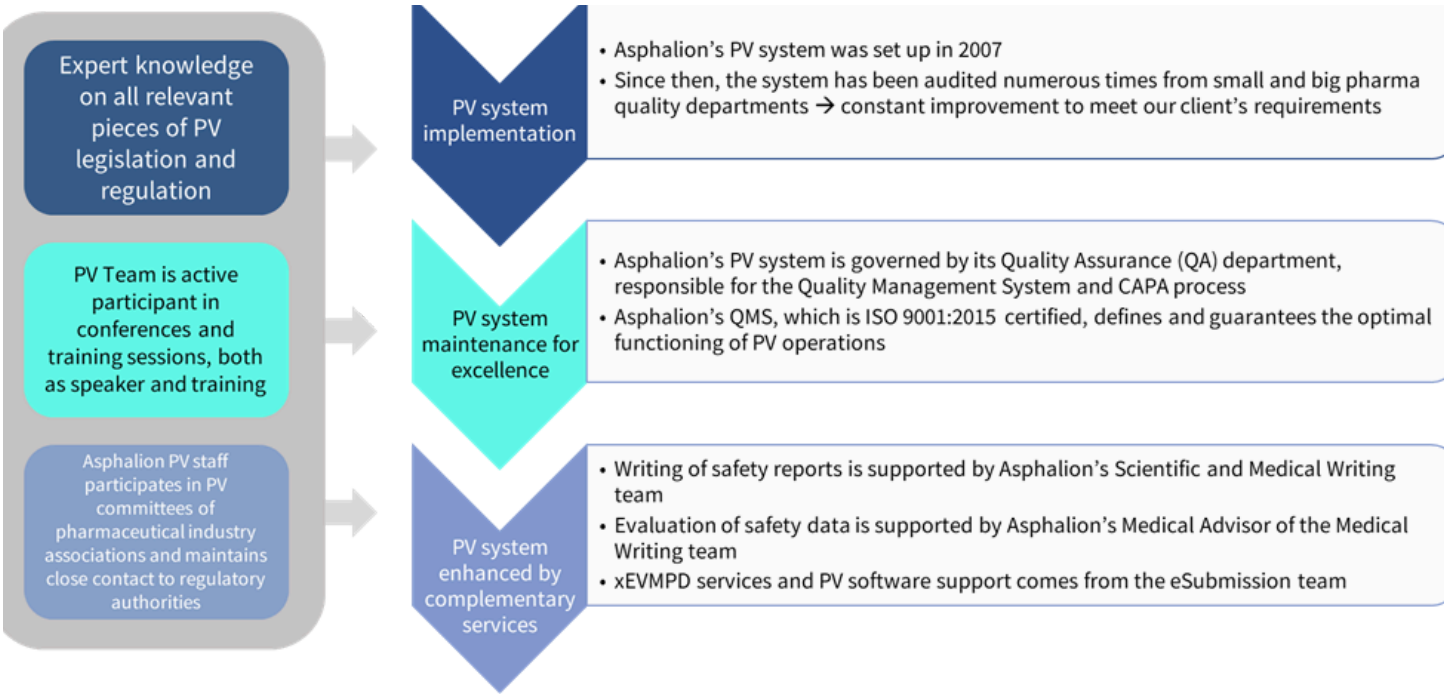
To stay compliant, MAHs should have a dynamic pharmacovigilance system that can adapt to the evolving requirements and maintain a proactive approach to monitoring safety literature both globally and locally.

3. About ASPHALION

ASPHALION is an international Regulatory, Scientific and Safety Consulting in Life Sciences with offices in Barcelona, Madrid, Pamplona, Munich and London.

Founded in 2000, ASPHALION has grown consistently and currently employs over 180 team members from 16 different nationalities.

Asphalion is an expert service provider in the field of PV for more than 15 years. As of today, Asphalion is providing PV services to over 160 clients, some of them long lasting collaborations, including the full outsourcing of the PV responsibilities.



3.1. Introducing AsphaNet

ASPHANET
Pharmacovigilance & Regulatory Affairs
European Local Contact Network

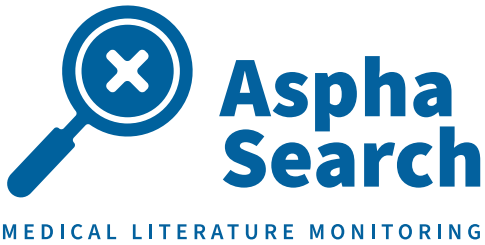
ASPHANET is our network of qualified partners that allows us to provide pharmacovigilance and regulatory affairs services throughout Europe

To help clients manage European pharmacovigilance from a single point, saving time and resources, Asphalion established its own partner network, AsphaNet. This network provides global, standardized local PV support under the oversight of an Asphalion pharmacovigilance expert, ensuring improved outcomes.

Through AsphaNet, Asphalion can offer its clients, through a centralized working model, all the necessary support in the different European countries, acting as a central coordination hub for all local pharmacovigilance activities. Our European network is composed of local companies with a wide experience in pharmacovigilance in the respective countries of operation, with strong knlowledge of the requirements, preferences and know-how of the different Pharmacovigilance National Competent Authorities.

To ensure that all our partners meet the same quality standards, they are all qualified and audited by Asphalion's quality team.

3.2. Introducing AsphaSearch



Automated literature search speeds up information retrieval using predefined search queries and replaces time-consuming manual processes. AI technologies facilitate the categorization of articles and the analysis of relevant safety data.

AsphaSearch is our validated, AI-based tool that uses artificial intelligence to perform local literature searches, facilitating articles categorization and analysis of relevant safety data.

This fully regulatory compliant software, enables local literature monitoring screening in more than 600 journals, with data storage enabled by Amazon Web Services, keeping audit trails in line with medicinal products lifecycle requirements.

It also allows articles translation and generation of automated reports and consequently, this tool allows the centralization of the local literature searches directly in Asphalion.

In conclusion, **AsphaSearch** allows us to perform local literature searches in more than 50 countries, with the advantages of:

- **Enhanced Efficiency**: Conducting simultaneous searches across multiple databases without incurring in additional costs.
- **Focus on value**: Ensuring precision and depth in searches, with a dedicated focus on safety data analysis.
- **Unwavering Quality**: Upholding the excellence that defines us, now fortified with advanced capabilities.

REFERENCES:
https://www.ema.europa.eu/en/documents/other/information-member-states-requirement-nomination-pharmacovigilance-phv-contact-person-national-level_en.pdf

ASPHALION
Knowledge from experience

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