# Basic module WiDi Pharma Deutschland (PD) Service on joint literature screening

According to the legal requirements laid down in the EU Directive 2001/83/EG as amended a MAH has the obligation to screen the scientific literature based on the active ingredients of its products on a weekly basis. Detailed guidance on the obligation is described in the Module VI of the “Good Pharmacovigilance Practices” (GVP). To fulfil this task the WiDi PD (Scientific and Economic Service of Pharma Deutschland) established a joint service on regular literature screening in 2003. The service is performed by two experienced service providers, namely PharmaLex GmbH, 61352 Bad Homburg, and Bremer Pharmacovigilance Service GmbH (BPS), 28327 Bremen, and is accompanied by the WiDi PD as a working group. The results of both service providers are presented by using PharmaLex´ internet-based platform Vigilit® and BPS´ internet-based platform Pharsalit.

Within the service PharmaLex is responsible for weekly screening of PubMed regarding chemically defined substances. BPS is responsible for weekly screening of herbal, homeopathic and anthroposophic substances in PubMed Both service providers assess the screened articles for their relevance of the drugs, substances or products’ safety and benefit-risk relation.

The Vigilit® Pharmacovigilance Literature Management and Retrieval System was developed by PharmaLex GmbH in 2002/2003; the Pharsalit system by BPS GmbH since end of 2005. Both service providers are regularly audited and certified by a group of experts under the control of DQS GmbH to ensure that the technical and executive realisation meets the contractual requirements.

The service supports the clients with ICSR reports and corresponding E2B-compliant xml files by sending them out via an automated mail-service (Vigilit® and/or Pharsalit push-service) which guarantees immediate delivery of the report after creation and medical review and release on a daily basis. The system also allows individual client searches for drug-related references (e.g. PSUR-relevant safety information. Ordering of full text articles included in the Vigilit® database can be performed via vigilit.info@smartphlex.com. Ordering of full text articles included in Pharsalit can be performed via pharsalit@bps-bremen.eu. Literature references are included from January 2022 in general in Vigilit® and from April 2003 in Pharsalit. New references are continuously uploaded to Vigilit® and Pharsalit. With the start of the EMA MLM-Service for a defined set of substances in September 2015, BPS offers an integrated daily service for the MLM case reports which meets the search strategy of the screened substances. This service contains daily retrieval, substance matching, version control and daily Pharsalit push-service with XML-E2B and readable safety report files.

The service workflow is based on corresponding SOPs, working instructions and includes the roles of Managers and specialists Pharmacovigilance at both service providers, who are qualified and appropriately trained to perform the assigned workflow steps. Literature screening in the above-mentioned databases is done on a weekly basis.

Each search cycle covers the data entered into the databases in a determined previous time period laid down in SOPs and working instructions of both service providers. Specific search terms, algorithms and qualifiers listed in corresponding templates/the database are employed in the searches. The retrieved references are then classified by appropriate trained managers or specialists into four categories, which distinguish adverse drug reactions (ADRs) as well as safety and efficacy information. ICSR including E2B compliant files are prepared for all references that are related to adverse drug reaction reports and are processed within seven calendar days and made available on day eight after identification of the minimum criteria (patient, adverse reaction, suspected drug, reporter) at the latest. If no full text article as information source can be obtained timely via an external literature provider, initial ICSR/E2B documents are prepared and will eventually be followed by final documents after receipt of the full texts. ICSR are prepared, medically reviewed and checked for correctness and appropriate coding of adverse reaction terms by managers. The uploaded ICSR and E2B files are immediately displayed to the client in Vigilit® and/or Pharsalit and also sent out by the above-mentioned push-service on the day after upload to the Vigilit® and/or Pharsalit internet application.

The systems of both service providers as well as the Vigilit® and Pharsalit system for presentation and archiving of the screening results are validated by extensive testing of each aspect of the functionality. Change requests to the system are done in corresponding change management systems, in order to facilitate the traceability of the changes applied to the system for improvement of functionality and specifications. Documentation of the workflow and the responsible parties is done both electronically and automatically in the system, providing exact information in the audit trail on every single action. Case documentation as well as documentation of the searches performed, permit to follow the whole course of a case from the beginning of the searches to the final report and make it possible to comprehend the involved persons and their responsibilities.

Both, the Vigilit® and Pharsalit systems are accessible via internet and have been stable and easy to use from the very beginning. Quality control tasks as well as security backups are performed on an ongoing basis in order to guarantee data security and integrity. Extension of the processed data and evaluation of further client’s needs and specifications put the system under an ongoing development, reflecting current pharmacovigilance requirements and discussions.

The screening of the EMA MLM service results and the reconciliation is performed by company according to internal SOPs.

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| **System name** | **Version\*** | **Vendor** |
| Vigilit | 7 | PharmaLex |
| Pharsalit | 3 | BPS |

\*Main effective version is reflected

# Extended module WiDi PD Service on joint literature screening including MLM@Vigilit

According to the legal requirements laid down in the EU Directive 2001/83/EG as amended a MAH has the obligation to screen the scientific literature based on the active ingredients of its products on a weekly basis. Detailed guidance on the obligation is described in the Module VI of the “Good Pharmacovigilance Practices” (GVP). To fulfil this task the WiDi PD (Scientific and Economic Service of Pharma Deutschland) established a joint service on regular literature screening in 2003. The service is performed by two experienced service providers, namely PharmaLex GmbH, 61352 Bad Homburg, and Bremer Pharmacovigilance Service GmbH (BPS), 28327 Bremen, and is accompanied by the WiDi PD as a working group. The results of both service providers are presented by using PharmaLex´ internet-based platform Vigilit® and BPS´ internet-based platform Pharsalit.

Within the service PharmaLex is responsible for weekly screening of PubMed regarding chemically defined substances. BPS is responsible for weekly screening of herbal, homeopathic and anthroposophic substances in PubMed. Both service providers assess the screened articles for their relevance of the drugs, substances or products’ safety and benefit-risk relation.

The Vigilit® Pharmacovigilance Literature Management and Retrieval System was developed by PharmaLex GmbH in 2002/2003; the Pharsalit system by BPS GmbH since end of 2005. Both service providers are regularly audited and certified by a group of experts under the control of DQS GmbH to ensure that the technical and executive realisation meets the contractual requirements.

The service supports the clients with ICSR reports and corresponding E2B-compliant xml files by sending them out via an automated mail-service (Vigilit® and/or Pharsalit push-service) which guarantees immediate delivery of the report after creation and medical review and release on a daily basis. The system also allows individual client searches for drug-related references (e.g. PSUR-relevant safety information. Ordering of full text articles included in the Vigilit® database can be performed via vigilit.info@smartphlex.com. Ordering of full text articles included in Pharsalit can be performed via pharsalit@bps-bremen.eu. Literature references are included from January 2022 in general in Vigilit® and from April 2003 in Pharsalit. New references are continuously uploaded to Vigilit® and Pharsalit. With the start of the EMA MLM-Service for a defined set of substances in September 2015, BPS offers an integrated daily service for the MLM case reports which meets the search strategy of the screened substances. This service contains daily retrieval, substance matching, version control and daily Pharsalit push-service with XML-E2B and readable safety report files.

Since July 2015 Pharmalex provides the MLM@Vigilit service. ICSRs provided by the EMA MLM service are screened by PLx and relevant ICSRs are provided via email. Therefore, a list of the EMA MLM screening results (Sum\_Screen) and a list of the ICSRs identified in the articles (Sum\_ICSR) are downloaded through the EVWEB portal of Eudravigiliance on a daily basis. All new identified ICSRs present in Sum\_ICSR as well as FU information are entered in a Master Excel Sheet. Newly identified relevant cases are downloaded via EVWEB. The cases are sent out via email (XML files as well as readable file) by PLx. The Master Excel Sheet is reviewed on a daily basis on correctness and completeness. MLM cases instead of own created cases are provided via Vigilit® if the respective case was created by MLM service. Therefore, a duplicate check of the Vigilit® case is performed against the Master Excel Sheet before a case is uploaded into the Vigilit® System.

The service workflow is based on corresponding SOPs, working instructions and includes the roles of Manager and specialists Pharmacovigilance at both service providers, who are qualified and appropriately trained to perform the assigned workflow steps. Literature screening in the above-mentioned databases is done on a weekly basis.

Each search cycle covers the data entered into the databases in a determined previous time period laid down in SOPs and working instructions of both service providers. Specific search terms, algorithms and qualifiers listed in corresponding templates are employed in the searches. The retrieved references are then classified by appropriate trained managers or specialists into four categories, which distinguish adverse drug reactions (ADRs) as well as safety and efficacy information. ICSR including E2B compliant files are prepared for all references that are related to adverse drug reaction reports and are processed within seven calendar days and made available on day eight after identification of the minimum criteria (patient, adverse reaction, suspected drug, reporter) at the latest. If no full text article as information source can be obtained timely via an external literature provider, initial ICSR/E2B documents are prepared and will eventually be followed by final documents after receipt of the full texts. ICSR are prepared, medically reviewed and checked for correctness and appropriate coding of adverse reaction terms by managers. The uploaded ICSR and E2B files are immediately displayed to the client in Vigilit® and/or Pharsalit and also sent out by the above-mentioned push-service on the day after upload to the Vigilit® and/or Pharsalit internet application.

The systems of both service providers as well as the Vigilit® and Pharsalit system for presentation and archiving of the screening results are validated by extensive testing of each aspect of the functionality. Change requests to the system are done in corresponding change management systems, in order to facilitate the traceability of the changes applied to the system for improvement of functionality and specifications. Documentation of the workflow and the responsible parties is done both electronically and automatically in the system, providing exact information in the audit trail on every single action. Case documentation as well as documentation of the searches performed, permit to follow the whole course of a case from the beginning of the searches to the final report and make it possible to comprehend the involved persons and their responsibilities.

Both, the Vigilit® and Pharsalit systems are accessible via internet and have been stable and easy to use from the very beginning. Quality control tasks as well as security backups are performed on an ongoing basis in order to guarantee data security and integrity. Extension of the processed data and evaluation of further client’s needs and specifications put the system under an ongoing development, reflecting current pharmacovigilance requirements and discussions.