Guidance on qualified person responsible for pharmacovigilance (QPPV) including pharmacovigilance system master files (PSMF) in a no-deal Brexit

Pharmacovigilance system requirements if there is a no-deal Brexit.

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Contents

The following legal obligations will apply to marketing authorisation holders (MAH) in the UK, in a no deal scenario:

- To operate a pharmacovigilance system for UK authorised products.
- To have an appropriately qualified person responsible for pharmacovigilance (QPPV) that resides and operates in the UK and is responsible for the establishment and maintenance of the pharmacovigilance system for UK authorised products (“the UK QPPV”).
- To maintain and make available upon request a pharmacovigilance system master file (PSMF) that describes the pharmacovigilance system for UK authorised products (“the UK PSMF”). The

UK PSMF must be located in, or accessible electronically from, the UK at the same site at which adverse reaction reports may be accessed.

The purpose of this guidance is to provide practical information and instructions to UK MAHs on:

- the role and responsibilities of the UK QPPV
- the development and registration of the UK PSMF and
- the notification of the summary of pharmacovigilance system to the Medicines and Healthcare products Regulatory Agency (MHRA).

Guidance on the UK QPPV

Role and responsibilities of the UK QPPV

The role and responsibilities of the UK QPPV are equivalent to that of the EU/EEA QPPV. In accordance with The Human Medicines Regulations (HMR) regulation 182(2) (as amended by The Human Medicines (Amendment etc.) (EU Exit) Regulations 2019 ("the EU Exit Regulations")), the holder must:

(a) have permanently and continuously at its disposal an appropriately qualified person responsible for pharmacovigilance who is ordinarily resident, and operates, in the United Kingdom and is responsible for the establishment and maintenance of the pharmacovigilance system.

Furthermore, HMR Schedule 12A (inserted by the EU Exit Regulations) paragraph 10(4) states:

The holder must ensure that the qualified person responsible for pharmacovigilance has sufficient authority to influence the performance of the quality system and the pharmacovigilance activities of the holder.

Further guidance on the qualifications and role of the EU/EEA QPPV is described in Good Pharmacovigilance Practice (GVP) Module I – Pharmacovigilance systems and their quality systems.

Temporary exemption as to the location of the UK QPPV

There is a temporary exemption in place which allows you until 21 months after exit day to appoint a UK QPPV that resides and operates in the UK. This is stated in section 1.9 of the further guidance from January 2019.

This temporary exemption will allow the EU/EEA QPPV who, immediately before exit day, resided and operated in an EEA state, to assume responsibility for UK authorised products until a QPPV who resides and operates in the UK can be established.

Guidance on the UK PSMF

UK PSMF location

You need to ensure that the UK PSMF is located at the same point in the UK from which the reports of suspected adverse reactions referred to in HMRregulation 187(4) are accessible (electronically or physically). This differs from the EU concept where the EU PSMF shall be located either at the site where the main pharmacovigilance activities are performed or at the site where the EU/EEA QPPV operates.

The UK PSMF needs to be permanently and immediately available for inspection at the stated location in the UK.

UK PSMF format, content and representation of PV systems

The requirements for the format and content of the UK PSMF are equivalent to that of the EU PSMF. The minimum requirements for the content and maintenance of the UK PSMF are laid out in HMR Schedule 12A and further guidance on the format and content of the EU PSMF is described in GVPModule II – Pharmacovigilance system master file.

The UK PSMF must describe the global pharmacovigilance system and reflect the global availability of safety information for UK authorised products. The annex content should be specific to UK authorised

products. As per GVP Module II, there are different approaches to establishing a pharmacovigilance system. For example:

- MAHs can establish more than one pharmacovigilance system.
- A pharmacovigilance system can be shared by several MAHs.

You must make sure that every pharmacovigilance system covering UK authorised products is identified by a unique number.

How to request a UK PSMF number

All UK PSMFs must be registered with the MHRA. You should request a unique UK PSMF number from the MHRA for each pharmacovigilance system that you are operating for UK authorised products. Where the pharmacovigilance system is shared by several MAHs, a single request for a UK PSMF number should be submitted to the MHRA.

A UK PSMF number request form will be available on the MHRA website immediately after exit day in a no deal Brexit scenario.

You should not request a UK PSMF number until you are planning to update the summary of pharmacovigilance system (SPS) for your UK product licences (PL) via submission of a variation application.

You should follow the instructions for completing the form and submit to: UKPSMFadmin@mhra.gov.uk

You will receive a unique UK PSMF number by email within 10 working days.

Notification of UK QPPV and PSMF details to the MHRA by existing holders of UK marketing authorisations (MA)

All UK MAs must include a summary of the holder's pharmacovigilance system, including the UK PSMF number. You should submit Type IAIN

variations related to the SPS to the MHRA and these submissions should cover all UK PLs under a unique pharmacovigilance system.

How to make your submission

All applications to update the SPS are required to be submitted as a Type IAIN - C.I.8.a variation via the MHRA Submissions portal.

In a no deal scenario we are expecting a large volume of regulatory submissions. You should submit your SPS updates as single changes and, to prevent delays, you should submit in collections of no more than 25 PLs.

Documentation you need to supply

You should supply the following documentation in a C.I.8.a submission (Introduction of, or changes to, a summary of pharmacovigilance system for medical products for human use):

1. Summary of the pharmacovigilance system, or update of the relevant elements (as applicable):

- Proof that the applicant has at his disposal a qualified person responsible for pharmacovigilance and a statement signed by the applicant to the effect that the applicant has the necessary means to fulfil the tasks and responsibilities listed in Part 11.
- Contact details of the appropriately qualified person who is ordinarily resident and operates in the UK (or those of the EU/EEA QPPV if this individual has assumed responsibility for UK MAs in the transitional period).
- A reference to the location where the PSMF for the medicinal product is kept or, if kept in electronic form, from which it can be accessed, which in either case must be in the United Kingdom.

2. UK PSMF number

Failing to supply all required documentation and information may lead to a rejection of the submission, which will require you to make a

resubmission addressing all discrepancies. The requirements for various categories of variations are outlined in the guidelines published by the Commission under Article 4 of Regulation (EC) No 1234/2008. UK specific requirements regarding the summary of the pharmacovigilance system are outlined in HMRSchedule 8.

Submission timeframes

You must notify the MHRA of changes to the SPS following the registration of the UK PSMF and any changes to the UK QPPV. The submission of SPSdetails for licences that were authorised via the EU centralised procedure should be handled differently to UK national licences. Please refer to this diagram which has an overview of the timeframes for submitting SPS details to the MHRA (PDF, 14.7KB, 1 page) but further details for the different licence types are provided below.

Guidance relating to UK national licences (including those authorised via mutual recognition or decentralised procedures)

On the day the UK leaves the EU, if the identity, location and contact details of the UK QPPV are identical to that of the EU/EEA QPPV immediately prior to exit day (as entered in the eXtended Eudravigilance Medicinal Product Dictionary, XEVMPD), no immediate action is required to notify the licensing authority.

Within two weeks of a change of identity, location or contact details of the UK QPPV (either a change in the QPPV resident in an EEA State or the introduction of a QPPV that resides and operates in the UK), you should submit a single change Type IAIN - C.I.8.a variation covering all UK PLs under a unique pharmacovigilance system (in collections of no more than 25 PLs).

A QPPV that resides and operates in the UK must be established within 21 months of exit day. If there is no change to the QPPV details from those entered on XEVMPD, then these details for the UK QPPV, together with the UK PSMF location and number, should be submitted as a single change Type IAIN - C.I.8.a variation before this deadline.

Licences authorised via the EU centralised procedure

All existing MAs authorised through the centrally authorised procedure will automatically be converted into UK MAs and issued with a UK MA number on exit day, in a no deal scenario.

You will have a period of one year, starting on exit day, to submit the initiating sequence data and related information in eCTD format.

Following submission of the initiating eCTD sequence and receipt of the approval letter from the MHRA:

- If the identity, location and contact details of the UK QPPV are identical to that of the EU/EEA QPPV immediately prior to exit day (as entered in XEVMPD), no immediate action is required to notify the licensing authority. Within two weeks of a change of identity, location or contact details of the UK QPPV (either a change in the QPPV resident in an EEA State or the introduction of a QPPV that resides and operates in the UK), you should submit a single change Type IAIN - C.I.8.a variation covering all UK (ex-EU) PLs under a unique pharmacovigilance system (in collections of no more than 25 PLs)
- If the identity, location or contact details of the UK QPPV are different to that entered in XEVMPD (either a change in the QPPV resident in an EEAState or the introduction of a QPPV that resides and operates in the UK), you should submit a single change Type IAIN - C.I.8.a variation covering all UK (ex-EU) PLs under a unique pharmacovigilance system (in collections of no more than 25 PLs)

Guidance for applicants for UK MAs

As per HMR Schedule 8, the material to accompany an application for a UK marketing authorisation includes a summary of the applicant's pharmacovigilance system which must include the following elements:

1. proof that the applicant has at the applicant's disposal an appropriately qualified person responsible for pharmacovigilance who is ordinarily resident, and operates, in the United Kingdom (or in

an EEA State if the EU/EEA QPPV has assumed responsibility for UK MAs in the transitional period)

2. the contact details of the appropriately qualified person
3. a statement signed by the applicant to the effect that the applicant has the necessary means to fulfil the tasks and responsibilities listed in Part 11
4. a reference to the location where the pharmacovigilance system master file for the medicinal product is kept or, if kept in electronic form, from which it can be accessed, which in either case must be in the United Kingdom

The SPS should also include the UK PSMF number.

Guidance on the application process is available.

Queries

General queries relating to the UK QPPV, UK PSMF and establishment of pharmacovigilance systems for UK authorised products should be sent to: gpvpinspectors@mhra.gov.uk
Queries relating to the UK PSMF number should be sent to: UKPSMFadmin@mhra.gov.uk
Queries relating to submission of Type IA variations should be sent to: variationqueries@mhra.gov.uk
This guidance will apply from exit day in line with the Human Medicines Regulations (Amendment etc.) (EU Exit) Regulations 2019.