Safeguarding public health

SME Workshop
"*Focus on Pharmacovigilance*"

GVP **Module II - Pharmacovigilance system master file**

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New legislation – provisions for PSMF

'Pharmacovigilance system master file: A detailed description of the pharmacovigilance system used by the marketing authorisation holder with respect to one or more authorised medicinal products'

The 2010 Directive and Regulation do not contain details on the content and maintenance of the PSMF.

Elements of PSMF content and maintenance are contained in the implementing measures (Regulation drafted), supplemented by the Good Vigilance Practices (GVP) guidance.

A single PSMF per pharmacovigilance system (*'one or more products')*

GVP Module II - Registration and Maintenance of PSMF

- **PV system summary**

  – article 8 of the Directive specifies that the QPPV contact details and the location of the PSMF must be included in the MA.

Note: although applicants for THMP registrations will not have to include a PV system summary in the application, article 104 still applies in that a PSMF will need to be made available and maintained.

Note: As well as for new MAA after 2/21 July, 2012, the introduction of the PV system summary applies in retrospect to products that undergo renewal.

Note: Even if the PV system summary is not required, a PSMF must be available for all products after the transition period (2/21 July 2015).

GVP Module II - Registration and Maintenance of PSMF

- **Location**
  – the site of the main pharmacovigilance activities or the QPPV, and must be within the Community

This must also be a physical address for the MAH or contracted third party, within the Union. Therefore, the most relevant EU site should be selected, the default being the QPPV site in the absence of an appropriate site for selection.

What considerations for guidance should be included for determination of 'main site' ?

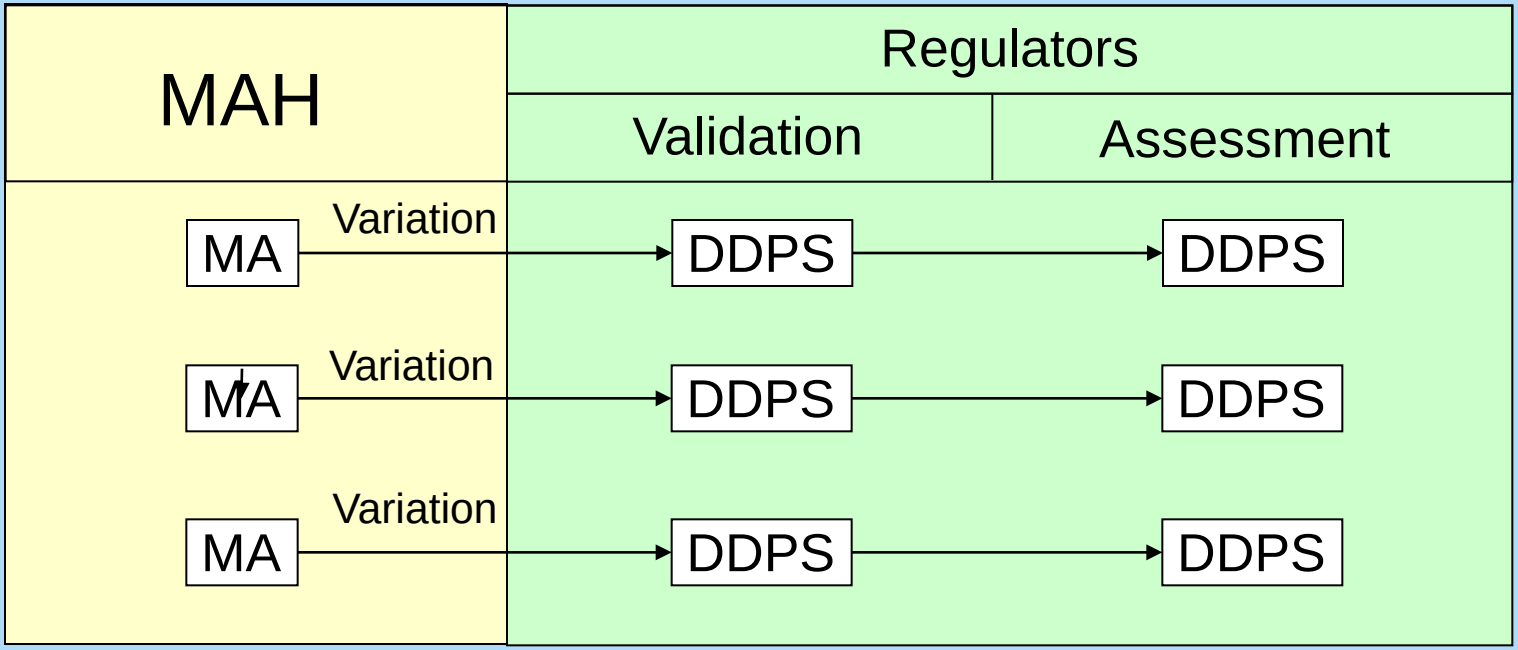
GVP Module II - Registration and Maintenance of PSMF

- **Registration**
  – In order to introduce a PSMF at times other than on marketing authorisation application or renewal, a variation must be submitted.

- **Transfer from DDPS**
  – introduction of the PSMF can occur voluntarily, earlier than renewal, pending which, DDPS requirements remain

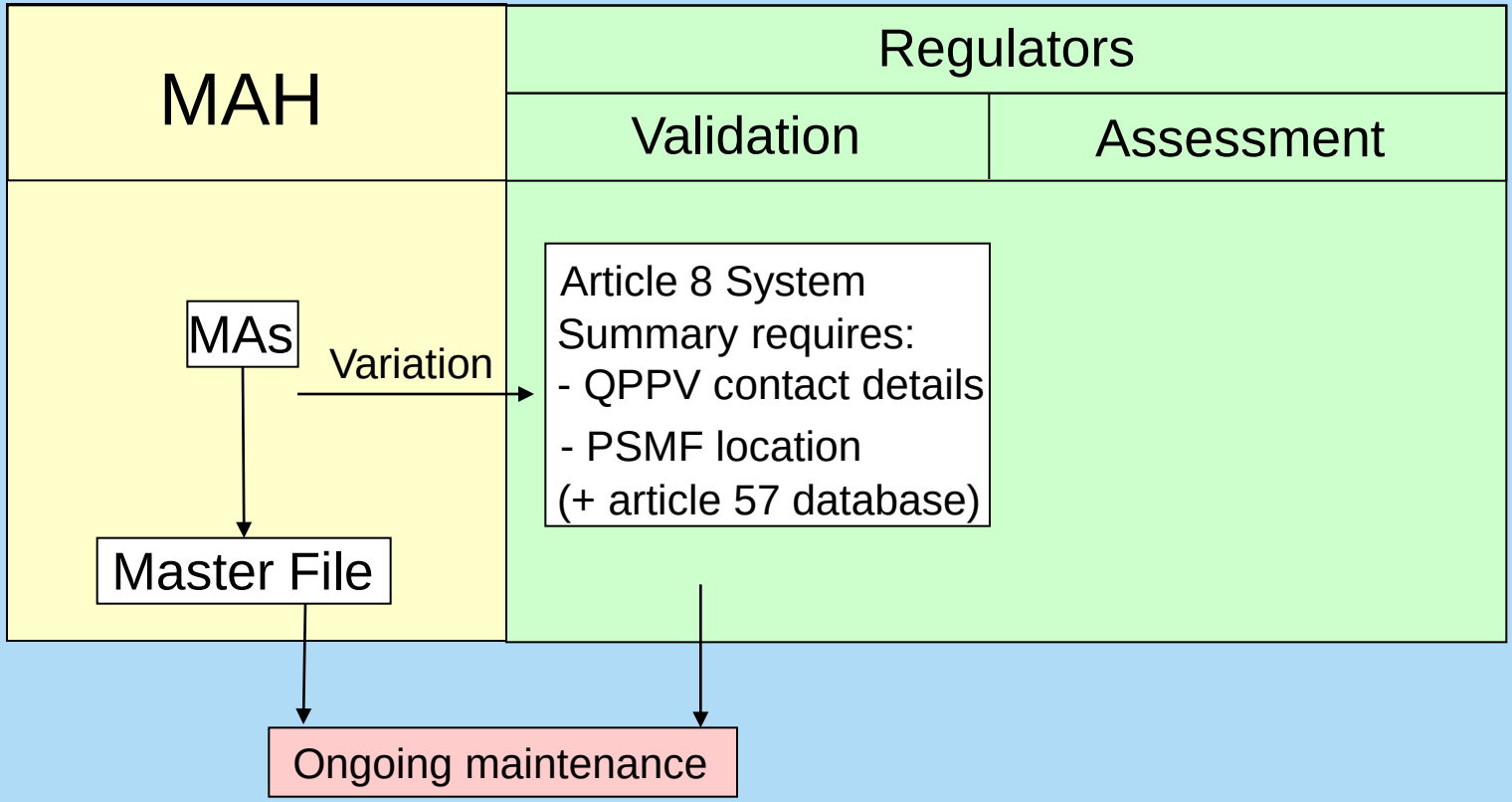
- **Variations**
  – the classification guideline is being amended to account for the introduction of the PSMF. After the initial introduction of the PSMF, changes to PSMF location and/or the QPPV must be submitted via variation (cross reference to the article 57 database), and are achieved practically by maintenance of the article 57 database fields.

Simplification – the concept (past)



Variations required for DDPS updates include: QPPV change, QPPV contact details change, back up of QPPV, change in the safety database, change in contractual arrangements, topics covered by written procedures, PV sites, (other) (*CI.9 of variations classification guideline)*

Simplification – the concept (future)



The PSMF will be kept up to date without variations. Variations will be required only for changes to the pharmacovigilance system summary (Article 8)

- **Early adoption of PSMF**

  - Where no renewal is due, it is possible for MAHs to include a PSMF location in the marketing authorisation by variation (and therefore be relieved of DDPS requirements where applicable).

  This can occur before the end of the transition period (before July 2015).

In the period up to 2015, what will be the voluntary uptake of PSMF?

What additional transitional guidance for the PSMF is required?

Module II – PSMF, Representation of PV systems

- Arrangements for shared systems and delegated activities are described

  - Single PSMF per system

  - Single location per PSMF

  - Possibilities of more than one system (and PSMF) per MAH

  - Defining responsibilities (and QPPV) for shared systems in written agreements

  - MAH able to provide information about the PV system (PSMFs) applicable to entire portfolio of MAs

What organisational arrangements and practical aspects do Industry want to see specifically covered in guidance?

Module II – PSMF, Information contained in the PSMF

The PSMF is modular, with descriptions and lists being organised to show change via a logbook or via change control of lists (annexes). The main contents are:

- QPPV details
- Products
- Organisational structure
- Sources of safety data
- Computerised systems and databases
- Processes
- PV system performance
- Quality System
- Logbook
- Annexes (lists)

The list formats are deliberately unspecified so that existing systems can be used to generate content, ***would Industry prefer a template approach?***

Module II – PSMF, the PV system and the QPPV

• **Objectives of the PSMF incorporate oversight**

'…the MAH and the QPPV should be able to:

- gain assurance that the PV system has been implemented in accordance with the requirements

- confirm aspects of compliance

- obtain information about the deficiencies in the system, or non-compliance with the requirements

- obtain information about risks or actual failures in the conduct of specific aspects of pharmacovigilance

The use of this information should contribute to the appropriate management of and improvement(s) to the pharmacovigilance system.'

Although there are no required variations, MAHs must still be prepared to submit PV system information and change information to allow NCAs and EMA to assess risk. This may be a full PSMF (including a pre-authorisation PSMF), the history of changes, or other relevant details)

• *The change control also supports the QPPV……*

Module II – PSMF, Change control and the QPPV

- **Informing QPPV and third parties/partners of significant changes:**

  - Safety database or associated databases, validation status (including data),
  - Service provision for pharmacovigilance,
  - Major contractual arrangements concerning PV,
  - Mergers, acquisitions,
  - PV sites, PSMF management.

- **Changes to be notified to the QPPV** are also in the section 'transfer of responsibilities':

  - Changes that must be submitted as variations,
  - The addition of corrective and/or preventative actions and managed deviations,
  - Changes that affect oversight of the PV system in terms of capacity, functioning and compliance,
  - Changes in the arrangements for providing the PSMF to NCAs,

- **Transfer of responsibilities for the PSMF** – the QPPV is to be informed, and must accept in writing the inclusion of new products in to the PV system, as well as responsibility for a PSMF (PV system).

Simplification – operational

•A uniform information set describing the pharmacovigilance system is available to the QPPV and for the purposes of audit.

•Tool for QPPV to oversee and manage system.

• There is a reduced burden in terms of documentation submitted as part of the MAA, for MAHs and NCAs: version control, storage.

•Less routine assessment of the system description: a practical reference for inspection and audit.

•There will be a harmonised and consistent PSMF for NCAs to use to plan inspections, MAHs will not necessarily need to manage ad hoc versions of pre-inspection documentation.

• Opportunity to use existing systems and to generate content for submission when requested.

What can we do to maximise the guidance?

Any questions?

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