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Requirements for systems for the performance of pharmacovigilance activities by Marketing Authorisation Holders, including the content and maintenance of the pharmacovigilance system master file

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*IMB Pharmacovigilance Information Day, 2<sup>nd</sup> Dec 2011*

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# Agenda

- **MAH Pharmacovigilance System**
  - Quality System (QS)
  - Pharmacovigilance System Master File (PSMF)
- **Quality Systems:**
  - Minimum requirements under consideration (*Sinead Curran*)
- **PSMF:**
  - Requirements for content and maintenance under consideration (*Majella Quinn*)
- **Aim:**
  - Key changes for MAH's
  - Report on Current Status



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# Quality and Pharmacovigilance

- Principles of Quality Systems are internationally recognised
- Current Framework:
  - Volume 9A of the Rules Governing Medicinal Products in the European Union
  - Provisions include requirements for training, QC/QA, documented procedures, audit.....
  - Approach taken not defined



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# New Framework: Standardisation of the Approach taken to Quality

**Directive 2010/84/EU**  
Requires uniform conditions



**Implementing Measure**  
min. requirements of the  
QS



**Good Vigilance Practice**  
Quality System Module  
PhV Inspection and Audit



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# Concept Paper on Pharmacovigilance Implementing Measures (1)



- **General Obligations:** Based on Quality Principles
- **Defined Aim:** Adequate and Effective for PhV activities
- **Scope:**
  - Organisational structure, responsibilities, procedures, processes, resources
  - Resource, compliance and record management
- **QS cycle:**
  - Structures and processes are planned and established
  - Carrying out tasks and responsibilities
  - Continuous monitoring and evaluation
  - Correction and improvement, as necessary
- **Documentation:** systematic and orderly manner
- **Audits:**
  - Performed at regular intervals
  - Personnel with no direct responsibility
  - Reported and reviewed by management



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# Concept Paper on Pharmacovigilance Implementing Measures (2)

- **MAH considerations:** Item for Consultation
- **Resource Management:**
  - Initial and continued training of personnel + QPPV
  - Organisational Structure, authority of QPPV
  - Business continuity planning
- **Compliance Management:**
  - Specific quality systems procedures and processes needed to assure compliance with key MAH obligations
- **Record Management:**
  - Retrievability, traceability
  - Retention period
  - Documentation arrangements, including location



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# Content and Maintenance of the Pharmacovigilance System Master File (PSMF)



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# Directive 2010/84/EC

- **Defines a Pharmacovigilance System as:**

*“A system used by the marketing authorisation holder and by Member States to fulfil the tasks and responsibilities listed in Title IX\* and designed to monitor the safety of authorised medicinal products and detect any change to their risk-benefit balance”*

- **Also states:**

- *The marketing authorisation holder should establish a pharmacovigilance system to ensure the monitoring and supervision of one or more of its authorised medicinal products, recorded in a **pharmacovigilance system master file** which should be permanently available for inspection.*
- *The competent authorities should undertake to supervise those pharmacovigilance systems.*



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# New Framework: PSMF

**Directive 2010/84/EU**  
Requirement for PSMF



**Implementing Measure**  
min. requirements for content &  
maintenance of PSMF



**Good Vigilance Practice**  
“Pharmacovigilance System  
Master File”



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# PSMF – Key Changes for MAHs

***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.


- Replaces the Detailed Description of the Pharmacovigilance System (DDPS), but maintains many of the same features.
- Not part of the MAA
- Summary of pharmacovigilance system provided in the MAA.



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# Summary of the Pharmacovigilance System

***2010/84/EC: “Applications for marketing authorisations should...be accompanied by a brief description of the corresponding pharmacovigilance system, which should include a reference to the location where the pharmacovigilance system master file for the medicinal product concerned is kept and available for inspection by the competent authorities”***

Detailed Description of the Pharmacovigilance System Current Directive 2001/83/EC	Pharmacovigilance System Master File Amendment from Directive 2010/84/EU
<p>Art 8(3)(ia) A detailed description of the pharmacovigilance and, where appropriate, of the risk-management system which the applicant will introduce.</p>	<p>Art 8(3)(ia) <b>A summary of the applicant’s pharmacovigilance system</b> which shall include the following elements:</p> <ul style="list-style-type: none"> <li>— <b>proof</b> that the applicant has at his <b>disposal a qualified person</b> responsible for pharmacovigilance,</li> <li>— the <b>Member States in which the qualified person resides and carries out his/her tasks,</b></li> <li>— the <b>contact details of the qualified person,</b></li> <li>— a statement signed by the applicant to the effect that the <b>applicant has the necessary means to fulfil the tasks and responsibilities listed in Title IX,</b></li> <li>— a reference to <b>the location where the pharmacovigilance system master file for the medicinal product is kept.</b></li> </ul>
<p>Art 8(3)(n) Proof that the applicant has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.</p>	<p>Point (n) is deleted;</p> <div style="text-align: right;">  <p>IRISH MEDICINES BOARD</p> </div>

# Points to note

- PSMF Location = at the site within the EEA where the QPPV operates
- An MAH/Company may have multiple PV systems therefore multiple PSMFs
- Any transfer of responsibilities for content & maintenance of PSMF must be documented
- PSMF must be permanently accessible, and provided within 7 days to authorities upon request.
- PSMF may be requested by NCAs/Agency during assessment of MA Applications (on an ad-hoc basis)



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# Structure + Content of the PSMF (1)

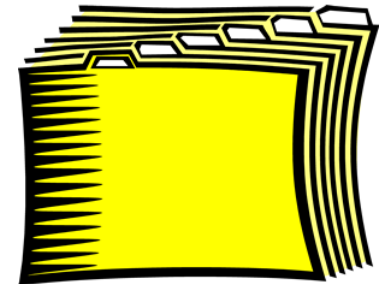
- Should be succinct, accurate, and current
- Current format = Paper or Electronic
- Contents include but not limited to:
  - List of relevant medicinal products
  - Cross reference to other PSMFs of the same MAH
  - QPPV details
  - Description of Organisational structure
  - Description of sources of safety information
  - Description of Databases
  - Contracts and agreements



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# Structure + Content of the PSMF (2)

- Description of processes, data-handling, and records in place for:
  - Continuous monitoring of benefit-risk
  - Risk management systems
  - ICSR collection, assessment and reporting
  - PSUR production and submission
  - Communications
- Description of Quality System for PV
- Description of Archiving
- Change History



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# Objectives of the PSMF

- Document the pharmacovigilance system and demonstrate compliance with the requirements
- Allow the MAH and the QPPV to maintain oversight of the system, particularly with respect to compliance and any potential deficiencies.
- Contribute to the appropriate planning and conduct of audits by the Applicant/MAH, and of inspections by national competent authorities
- Removes redundancy and paperwork in terms of submission and associated assessment of MAAs.
- Reduces burden of variations arising from changes to the system



# Registration & Maintenance of the PSMF

- Legislation = Transition to PSMF to occur:
  - at time of MA application,
  - or at time of renewal,
  - or by 21<sup>st</sup> July 2015 for existing MAs.
- Proposal = MAHs may make transition to PSMF for existing products prior to this on a voluntary basis, by variation.
- Variation required for changes to summary provided as part of the MAA (location, QPPV etc).
- Art 57 database will contain the QPPV/PSMF location and the QPPV's contact details. Proposal is to use the database for administrative updates (QPPV's contact details and change of address within the same country).
- All changes must be notified to the QPPV



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**Thank you**



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