Federal Agency for Medicines and Health Products
(FAMHP)

Implementation of new pharmacovigilance Directive and Regulation

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Plan

- New legal framework as regards pharmacovigilance of medicinal products for human use
- Implementation, delegation and guidance
- Key measures
- Legislation : main changes
- PRAC
- Union-wide assessment of phvig issues
- Strengthened transparency and communication

New legal framework as regards pharmacovigilance of medicinal products for human use

- Regulation (EU) No 1235/2010 of the European Parliament and of the Council of 15 December 2010 amending, as regards Pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products (specific provisions on centrally authorised products and EMA tasks)

- Directive 2010/84/EU of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use (nationally authorised products and common provisions)

⇨ Adopted by both Council and EU parliament and publication on 31 Dec 2010
⇨ Most of the provisions will come into force in July 2012

Implementation, delegation and guidance

- **Implementing Measures** – Dir. art. 108

= To harmonise the conduct of pharmacovigilance activities

→High level principles, legally binding at the top

  - Content and maintenance phvig master file, format and content PSUR and RMP, …

- **Delegated acts** – Dir. art. 22b

= Measures supplementing the provisions in Dir. Art. 21a and 22a

  - situations where post-authorisation efficacy studies may be required

- **Guidance** – Dir. art. 108a

= To facilitate the conduct of pharmacovigilance activities

  - guidance on good pharmacovigilance practices for CA and MAHs
  - scientific guidance on post-authorisation efficacy studies

Guidance

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Annex: Draft list of GVP Modules[2]

GUIDANCE ON GOOD PHARMACOVIGILANCE PRACTICES (GVP)

INTRODUCTION	Legal Basis and Structure of Pharmacovigilance Guidance
MODULE I	**Pharmacovigilance Systems and their Quality Systems**
MODULE II	**Pharmacovigilance System Master File**
MODULE III	Pharmacovigilance Inspections
MODULE IV	Audits
MODULE V	**Risk Management Systems**
MODULE VI	**Management and Reporting of Adverse Reactions to Medicinal Products**
MODULE VII	**Periodic Safety Update Reports**
MODULE VIII	**Post-Authorisation Safety Studies**
MODULE IX	**Signal Management**

Guidance

MODULE X	Additional Monitoring
MODULE XI	Public Participation in Pharmacovigilance
MODULE XII	Continuous Pharmacovigilance, Ongoing Benefit-Risk Evaluation, Regulatory Action and Planning of Public Communication
MODULE XIII	Incident Management
MODULE XIV	Referral Procedures for Safety Reasons
MODULE XV	Safety Communication
MODULE XVI	Tools, Educational Materials and Effectiveness Measurement for Risk Minimisation

PRODUCT- AND POPULATION-SPECIFIC CONSIDERATIONS

ANNEX I	**DEFINITIONS**
ANNEX II	TERMINOLOGY
ANNEX III	TEMPLATES
ANNEX IV	LIST OF INTERNATIONAL PHARMACOVIGILANCE GUIDANCE DOCUMENTS
ANNEX V	LIST OF OTHER GUIDANCE DOCUMENTS

Key measures

Strengthening and rationalizing the EU pharmacovigilance system

- Clear tasks and responsibilities for key responsible parties

- Collection of high quality data, while avoiding unnecessary administrative burden, through proactive and proportionate risk management planning

- Improved Community decision-making procedures
  - ✓efficient use of resources
  - ✓harmonised decisions
  - ✓stronger link between safety assessments and regulatory action

- Strengthened transparency and communication

Legislation : main changes

«OLD» LEGISLATION	«NEW» LEGISLATION
DDPS	Pharmacovigilance system master file
RMP if required	RMP for all applications (proportionate to risks)
Definition of ADR: under normal conditions	Definition of ADR: also in case of off label use, misuse,…
SERIOUS ADRs to EV	SERIOUS and NON SERIOUS ADRs to EV
Patient reporting: no legal basis	Patient reporting: legal basis
PSURs for all MAs	PSURs submission in function of risks
PSUR WS on voluntary basis	PSUR WS: legal basis

Legislation : main changes

«OLD» LEGISLATION	«NEW» LEGISLATION
Renewal submission 6 month before expiration of validity	Renewal submission 9 month before expiration of validity
Signal detection: no legal basis	Signal detection: legal basis
PASS: no legal basis	PASS: legal basis
PAES: no legal basis	PAES: legal basis
Additional monitoring: no legal basis	Additional monitoring: legal basis
PhVWP	PRAC New urgent union procedure More transparency
POST MA inspections	PRE and POST MA inspections and more focus on sharing information between CA

PRAC

New scientific committee within the Agency

Pharmacovigilance Risk Assessment Committee - Reg art. 56(1)(aa)

Mandate – Reg. art. 61a §6

" All the aspects of the risk management of medicines … having due regard to the therapeutic effect of the medicinal product …":

- Recommendations to CHMP and CMD(h) on Phvig issues
- Role in agreement and monitoring of RMPs
- Prioritisation and review of emerging safety signals
- Review of PSUR assessments
- Evaluation of protocols and results of PASS
- Decision on products under additional monitoring
- …

PRAC - composition

Appointed by each Member State:

- 1 member + alternate
- 27 + EEA countries non voting members

Appointed by the European Commission following a public call for expressions of interest:

- 1 patient organisations rep + alternate
- 1 healthcare professionals rep + alternate
- 6 members to ensure relevant expertise available

PRAC - activities

Activity	Involvement
Risk Management Systems	Agreement on RMPs + monitoring their effectiveness
Periodic Safety Update Reports PSURs	List of harmonised submission frequencies and substances, assessment + recommendation
Eudravigilance + Periodic Safety Update Reports repository	Functional specifications, any substantial changes
Medicines subject to additional monitoring	Addition to/removal from list, extension of timeframe, symbol
Signal Detection	Initial analysis + prioritisation assessment + recommendations

PRAC - activities

Activity	Involvement
Urgent Safety Procedures for the EU	Assessment, public hearings, recommendations
Post Authorisation Safety Studies	Consultations on requests (pre and post MA), assessment of protocols (incl. amendments) + recommendations, assessment of results + recommendations
Literature Adverse Drug Reactions monitoring	Consultation on list of active substances and medical literature subject to monitoring?
Safety announcements	Advice

PRAC

Interaction with CHMP and CMD(h)

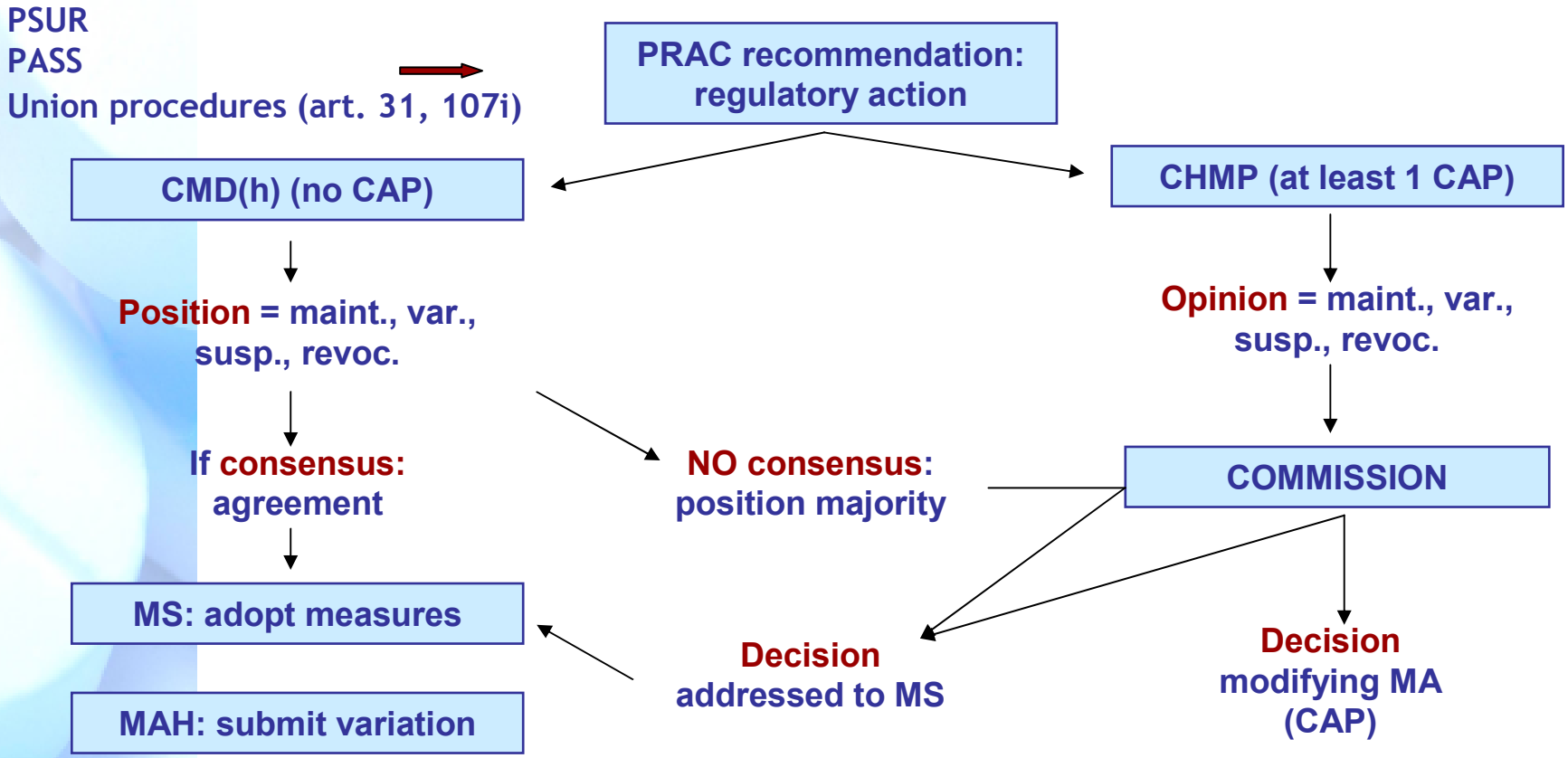
- **PRAC provides recommendations to CHMP and CMD(h)** – Reg. art. 56(1)(aa)

- **CHMP / CMD(h) shall rely on the scientific assessment and recommendations of PRAC for the fulfilment of its phvig tasks, including the approval of risk management systems and monitoring their effectiveness** – Reg. art. 5(2) / Dir. art. 27

- **Explanation on the scientific grounds for differences if opinion / agreement is not in accordance with PRAC recommendation**

PRAC

Decision-making process



Union-wide assessment of phvig issues

Two procedures for Union-wide post-authorisation assessment of PhVig issues

- Dir. art. 107i-l = **urgent** union procedure (revision current art. 107)
- Dir. art. 31 in other cases
- Dir. art. 36 deleted

⇨PRAC should always give its recommendation when the reason for taking action is based on PhVig data (regardless of whether centralised or non centralised procedures, urgent or normal procedure) – Dir. Cons (25a)

⇨Procedures laid down in Directive 2001/83/EC to be followed, also for centrally authorised products – Reg. cons. (9a)

Union-wide assessment of phvig issues

Urgent Union Procedure
Triggers - Dir. art. 107i

Urgent action necessary, as a result of the evaluation of phvig data. MS / Commission:

a. considers suspending or revoking a MA;
b. considers prohibiting the supply of a medicinal product;
c. considers refusing the renewal of a MA;
d. is informed by the MAH that, on the basis of safety concerns, he has interrupted the placing on the market of a medicinal product or withdrawn a MA, or that he intends to do so;
e. considers that new contraindications, a reduction in the recommended dose, or a restriction to the indications is necessary;

Union-wide assessment of phvig issues

Urgent Union Procedure
Scope of procedure - Dir. art. 107i

- Agency verifies scope: should cover all products concerned to ensure single assessment of the safety issue (other products? whole class / range?)
  - ⇨Agency shall extend scope if necessary (including CAP)

⇨If > 1 MS concerned: art. 107k-107l apply
⇨If only 1 MS concerned: issue addressed by MS

Union-wide assessment of phvig issues

Urgent Union Procedure

Procedure - Dir. art. 107i-l

- Initiation of procedure by MS or Commission
- Inform other MS, Commission, EMA
- Verification of scope (EMA)
  - MS may suspend, prohibit use on its territory until a definitive decision is adopted
  - Commission may take temporary measures or request MS to take temporary measures immediately
- Public announcement of initiation of procedure (EMA web-portal)
  - information on right for MAH, HCP, public to submit info to EMA
- PRAC assessment (MAH comments in writing / public hearing)
- PRAC recommendation

⇨CMD(h) / CHMP decision-making

Union-wide assessment of phvig issues

Urgent Union Procedure
Public hearing - Dir. art. 107k

- PRAC may hold public hearing
  - ✓if urgency allows
  - ✓justified grounds, particularly extent and seriousness of the issue
- announcement on EMA web-portal specifying modalities of participation

- EMA shall draw up rules for organisation / conduct - Reg. art. 78

- Possibility for MAH / public to request non-public hearing (if confidential data)

Strengthened transparency and communication

European and national (safety) web portals

National medicines web-portal – Dir. art. 106:

- summaries of RMP (national MA)
- list of medicinal products referred to in Article 23 of Reg.
- information on the different ways for reporting suspected ADRs, including the web-based structured forms (Reg. art. 25) ..

European medicines web-portal – Reg. art. 26:

- agendas and minutes from each meeting of the CHMP and PRAC and the CMD(h) as regards phvig activities
- summary of the RMP (CAP authorised products)
- Assessment conclusions, recommendations, opinions, agreements and decisions (for PSURs, urgent union procedure, PASS) taken by CHMP, PRAC, Commission, NCA and CMD(h)
- …

Strengthened transparency and communication

coordination safety announcements by EMA

Dir. art. 106a / Reg. art. 22

MAH:

- should provide the authorities with prior or simultaneous warning about safety announcements
- Information to the public is presented objectively and is not misleading

Member States, EMA and the Commission:

- inform each other not less than twenty-four hours prior to a public announcement (unless urgent)
- If more than 1 MS concerned: EMA coordination
  - MSs shall make all reasonable efforts (under coordination of EMA) to agree on common safety messages and the timetables for their distribution
  - PRAC (at the request of EMA): provide advice on those safety announcements

Strengthened transparency and communication

Product information (SmPC and PIL)

- No agreement on a "summary of essential information"
- But: Commission to present to EP / Council assessment report on shortcomings in SmPC / PIL + if appropriate proposals to improve readability, layout and content – Dir. art. 59 (3)

- For all medicinal products: standard text expressly asking HCP (Dir. art. 11) / patients (Dir. art. 59) to report any suspected ADR.
  Different ways of reporting shall be available

- Medicinal products for which additional monitoring standard text + black symbol

Thank You