EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

31 January 2011
EMA/58716/2011
Patient Health Protection

Planning for the Implementation of the New Legislation on Pharmacovigilance

Project 00305

1. Purpose

This document provides an outline of the arrangements put in place to prepare for the implementation of the new pharmacovigilance legislation. Particularly, it sets out:

1. The governance structure
2. A high level risk analysis
3. The key deliverables to be implemented
4. Project planning

2. Introduction

Following adoption by the European Parliament and the European Council, Regulation (EU) No 1235/2010 and Directive 2010/84/EU on pharmacovigilance were published in the Official Journal on 31 December 2010. Most of the provisions will come into force in 18 months following the publication (2 July 2012 for the Regulation and 21 July 2012 for the Directive).

This new public health legislation is far reaching in scope and in depth and goes far beyond any narrow concept of pharmacovigilance. The legislation strengthens safety monitoring, rationalises reporting and increases the use of studies including pharmacoepidemiology, makes clear roles and responsibilities, sets out decision-making, increases participation, reinforces transparency and strengthens the action that can be taken to protect and promote public health. Based on the European Commission (EC) impact assessment, the new legislation promises between 591 and 5910 lives saved per year across the EU and savings to society of between €237 Million and €2.4 Billion per year. While the EC proposals were amended in the co-decision procedure, the objectives and the key measures all remain.

The new legislation requires important changes to existing processes in the Member States, the European Medicines Agency (EMA) and Marketing Authorisation Holders (MAHs) and creates completely new processes. While the burden on the industry particularly for reporting suspected adverse reactions and for periodic safety update reports should be reduced, this simplification of reporting requires new resources at the EMA for its realisation since the coordinating role of the EMA is further strengthened.

The new legislation requires a set of legislative implementing measures from the EC and implementing guidelines from the EMA, in addition to the establishment and operation of new processes. The impact on the EMA and the EU Regulatory Network (the Network) is major and successful implementation and operation will require integrated, collaborative working between the EC, the EMA and the Member States.

3. Governance Structure

3.1. Rationale

Preparing for the implementation of the new pharmacovigilance legislation will require tasks to be carried out by the EC (such as adoption of implementing measures and delegated acts), and tasks to be carried out by the EMA. The aim of this document is to propose a governance structure for the tasks to be carried out by the EMA.

Taking into account the complexity of the Network as well as the number of (scientific) fora which are directly affected by the new legislation, there is a need for

- a coordinated approach in preparing for the implementation of the new legislative provisions for which the EMA is responsible;
- making best use of the available resources;
- avoiding unnecessary duplication of work.

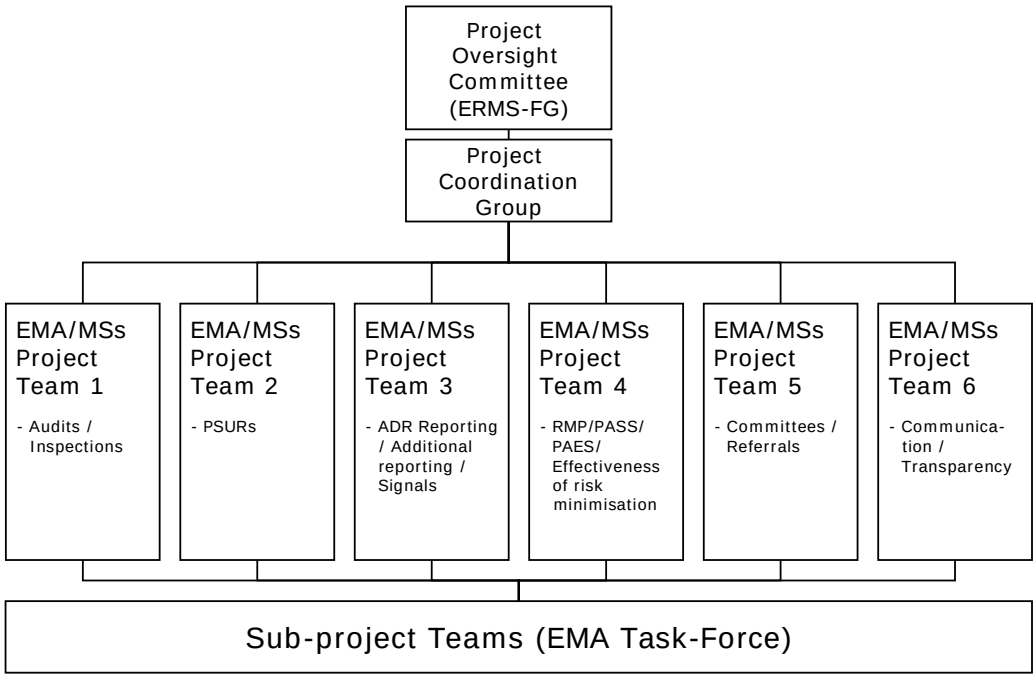
The availability of an appropriate governance structure to oversee and monitor the preparatory work for the entry into force of the new legislation will be an important prerequisite.

Several (scientific) fora are directly affected by the new legislative provisions: CHMP, PhVWP (to be replaced by the PRAC), CMD(h) and PhV IWG. In addition, some aspects of the implementation for tasks to be carried out by the EMA will require decision-making by fora such as the EMA Management Board and HMA, especially when strategic choices have to be made.

3.2. Governance Structure for EMA Tasks

Although the EMA has started to prepare for the implementation by establishing an internal Task Force in January 2010 (as is normally done for any new EU legislation impacting on the EMA), recent discussions have highlighted the need for a coordinated approach with the work undertaken by the EC and the Member States. Therefore, the following dedicated governance structure is set-up for the tasks carried out by the EMA:

Governance of the Planning for the Implementation of the New Pharmacovigilance Legislation for EMA Tasks



3.2.1. Establishment of a Project Oversight Committee

A Project Oversight Committee is established, composed of the EC, the EMA and the Member States (including representation from the aforementioned (scientific) fora).

The existing ERMS-FG (chaired by a HMA with involvement of the EC, the EMA and the PhVWP) will act as the Project Oversight Committee, but membership is broadened to include CHMP and CMD(h) representatives. The role of the ERMS-FG in the context of the preparation for the implementation of the new pharmacovigilance legislation is to oversee and monitor such preparation and to agree on the main deliverables (as outlined in Section 2.3 Working Methodology). The ERMS-FG will continue to report to HMA and the EMA will ensure that the output of the ERMS-FG is also reported to the EMA Management Board, where relevant.

This will require an amendment to the current remit of the ERMS-FG.

3.2.2. Establishment of a Project Coordination Group and EMA/Member States Project Teams

The ERMS-FG is complemented with six EMA/Member States Project Teams (each time co-chaired by an EMA and a Member State representative) covering particular fields of the new legislation. These Project Teams cover the following areas:

- Project Team 1: Audits / Inspections
- Project Team 2: PSURs
- Project Team 3: ADR reporting / Additional monitoring / Signals
- Project Team 4: RMP / PASS / PAES / Effectiveness of risk minimisation
- Project Team 5: Committees / Referrals
- Project Team 6: Communication / Transparency

As regards the composition of these Project Teams, membership will come from existing fora (such as the CHMP, PhVWP Drafting Groups, the CMD(h), the PhV IWG), "enriched" with the required expertise coming from other fora (such as the EudraVigilance Expert Working Group, the HMA/EMA Transparency Group). This will ensure both avoiding duplication of work and making use of the best expertise. Member State Co-Chairmanship of the EMA/Member States Project Teams is decided upon by HMA on a proposal made by the ERMS-FG. The EMA/Member States Project Teams are supported by existing EMA Sub-project Teams which have been set-up by the EMA Task Force in 2010.

Project coordination is undertaken by a (virtual) Project Coordination Group co-chaired by an EMA representative and the PhVWP Chair with involvement of the EMA/Member States Project Teams' Co-Chairs and any additional expertise as required. Further information on the mandates of the Project Coordination Group and the Project Teams is provided in Annex 1.

3.2.3. Working Methodology

Taking into account the vast amount of work which needs to be undertaken over the next 18 months, efficiency will be key to allow timely delivery. In addition, in view of the resources available prioritisation of work will be required leading to a stepwise implementation. This will necessitate discussion at the level of the ERMS-FG to allow decision-making by HMA and the EMA Management Board.

For each deliverable a Topic Lead or Rapporteur will be identified and in some cases a Co-Rapporteur. Deliverables will be discussed at the respective EMA/Member States Project Team and final agreement will be sought at ERMS-FG level. Involvement of existing fora such as CHMP, PhVWP, CMD(h) and PhV IWG will be undertaken as necessary prior to final agreement by the ERMS-FG. Formal adoption of deliverables may be by the EC, the Pharmaceutical Committee, the EMA, HMA or an EMA Scientific Committee, depending on the deliverable concerned and its status within the new pharmacovigilance legislation.

3.2.4. Stakeholder Liaison

Formal public consultation, where relevant, will be important to ensure effective interaction and dialogue with key stakeholders (such as pharmaceutical industry, patient groups, etc.). It is envisaged for up to 6 public fora to be held at the EMA in 2011 (depending on the available budget). To make best use of these public fora certain documents (e.g. papers to support decisions where key strategic and policy orientations are needed for implementation, pre-final deliverables) will be presented to stakeholders for discussion.

4. Project Risk Management

This section outlines the risks inherent to the implementation of the new legislation on pharmacovigilance, provides a qualitative estimation of their likelihood and impact, and describes mitigation actions. Throughout this phase, it is foreseen to regularly review all aspects related to the project's risks and provide updates to the project governance structure put in place.

It should be emphasised that the main risks impacting on a successful implementation relate to the availability of the necessary human, financial and IT resources.

Table Project Risk Management

Risk description	Likelihood	Impact	Risk mitigation measures
EMA and Member States do not deliver technical contribution on time for EC to adopt the implementing measures	Low	High	• Joint EMA/Member States technical contribution to the Implementing measures is planned to be delivered in Q2 2011. • Working methodology is described in the chapter on governance.
EMA and Member States do not implement the ***key*** measures within the 18-month legal deadline	Low	High	• Implementation Plan including checklist have been prepared and agreed. • Close monitoring on progress is foreseen. • Regular reporting on status and relevant risks to the project. • Oversight is foreseen.
EMA and Member States do not implement ***all*** measures within the 18-month legal deadline	High	Medium	• Governance will focus on ensuring that key measures are in place. • Prioritisation of other tasks to be carried out is foreseen.
Roles and responsibilities are unclear during the implementation phase	Low	Medium	• Overall project governance is defined. • Mandate has been prepared and agreed at project oversight level.
Inadequate cooperation and collaboration between all stakeholders involved in policy development	Low	High	• Project governance (involving ERMS-FG, CMD(h), PhVWP, CHMP, HMA, EMA Management Board) and working methodology have been agreed. • Close monitoring on progress. • Regular reporting on status and relevant risks to the project oversight is foreseen. • Stakeholder meetings have been planned in 2011.

Risk description	Likelihood	Impact	Risk mitigation measures
Inaccurate estimate of the EMA resources and budget required to implement the new legislation	Medium	High	• Impact evaluation established by EMA Task-Force. • Impact evaluation presented and agreed at the level of EMA Management. • Impact evaluation estimate taken into account in the EMA planning.
Inadequate resources (human and financial) available in 2012, 2013 and beyond	High	High	• EMA has evaluated impacts and costs for activities impacting on it and will include this in its yearly Working Programmes for decision by its Management Board. • Need for rapid introduction of new fees identified.
EMA subproject teams and EMA/MSs Project Teams do not provide IT business requirement on time for the EMA ICT Unit to prepare IT implementation and cost/resource planning	Medium	High	• IT business requirements are planned to be delivered in Q1 2011.
Inaccurate description of IT business requirements	Medium	High	• Governance to support the coordination of IT business requirements is established.
Agreed IT business requirements not implemented within the agreed timelines	High	High	• IT planning to be developed as soon as all IT business requirements are delivered in Q1 2011. • EMA making the case for appropriate funding.
EMA does not assess the impact of the implementation on its operations and business processes	Low	Medium	• Impact evaluation was conducted by EMA in 2010 and was used for 2011/2012 work plans • EMA business processes design is planned in Q1-Q2 2011. • EMA subproject teams will follow common guidance to design business processes. • Business processes design will involve all relevant Units within the EMA.
EMA does not finalise the documentation related to business processes	Low	Medium	• Preparation of documentation related to business processes has been planned.

5. Key Measures

Annex 2 provides a checklist of processes that need to be established and tasks that need to be performed for the implementation of the new legislation (EMA and Member States Joint Implementation Check-list). The check-list is necessarily high level in order to guide the initial planning and work initiation. It will be supplemented with more detailed identification of deliverables and milestones as the EMA/MSs Project Teams work progresses.

6. Project Planning

This section provides information on the project planning. It serves as a baseline to be revised and updated as necessary.

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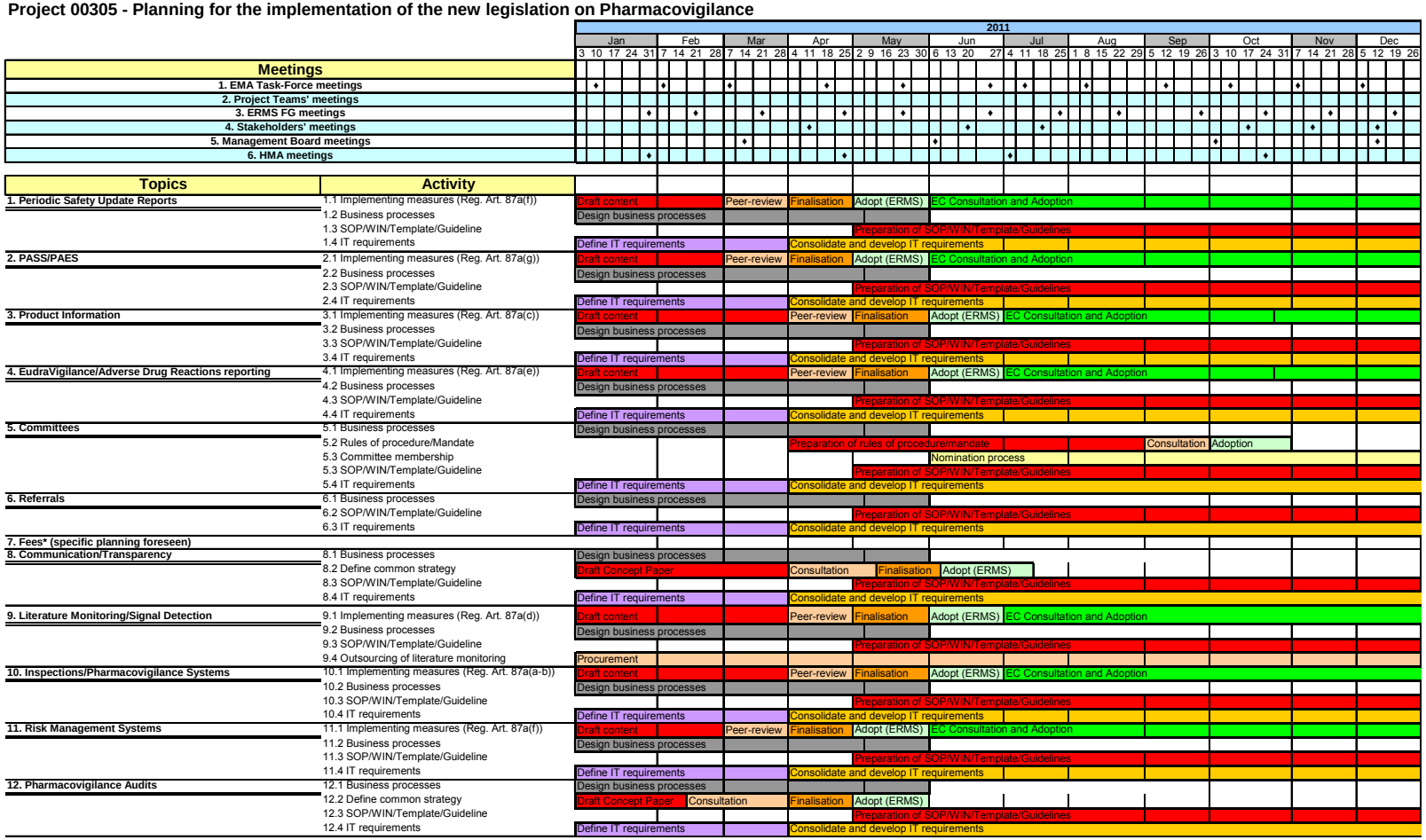

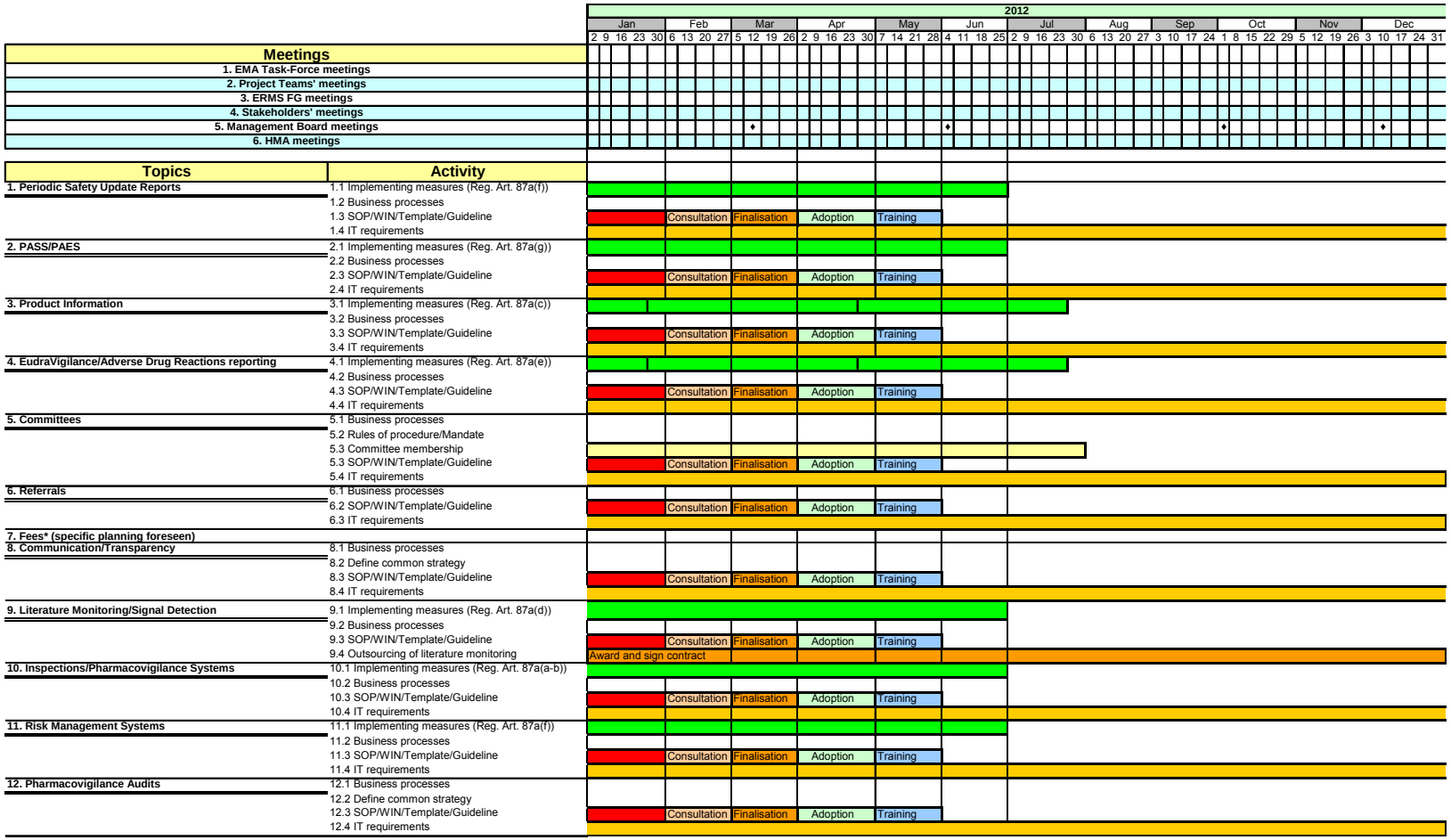
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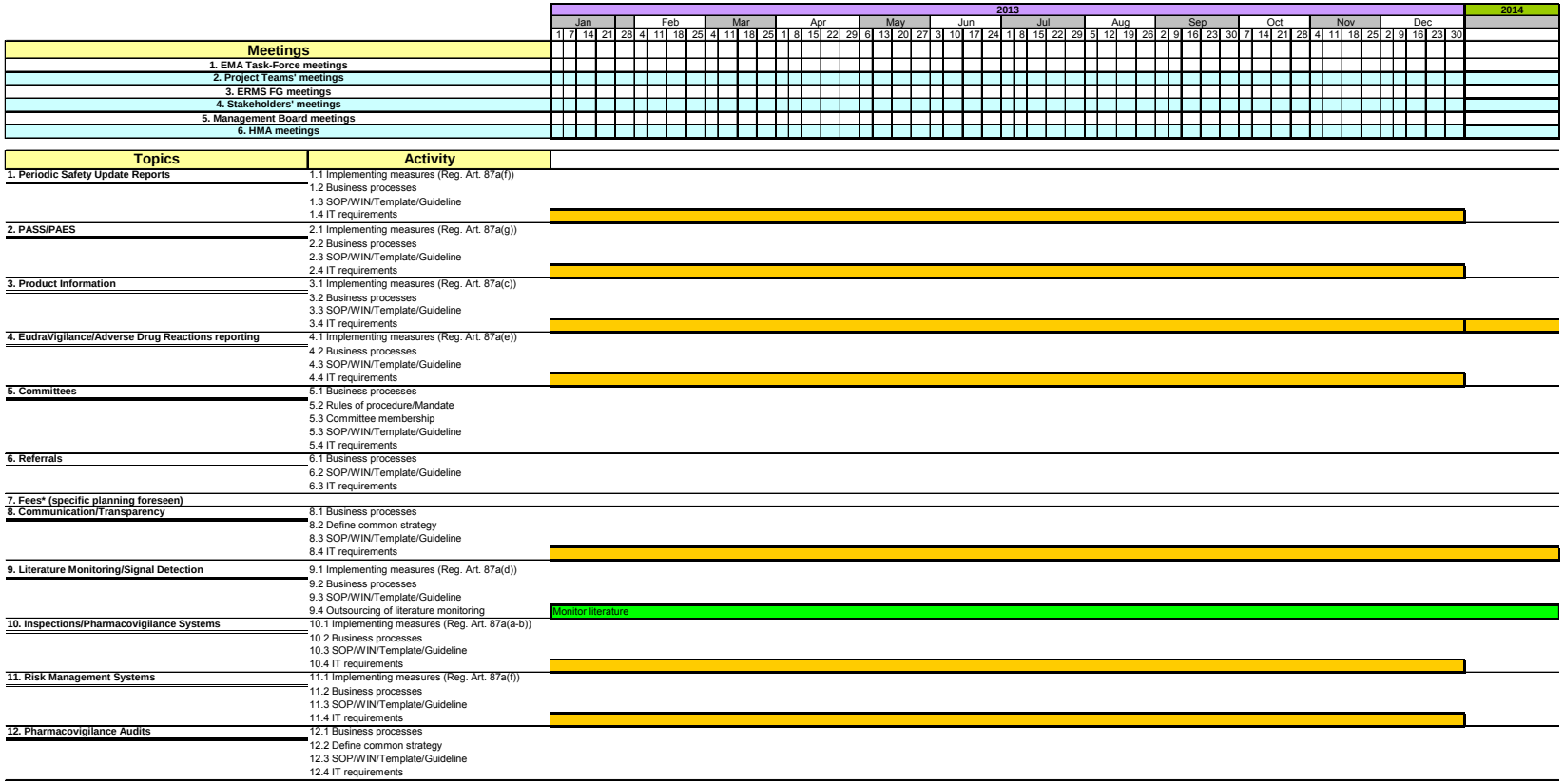
Meetings
1. EMA Task-Force meetings
2. Project Teams' meetings
3. ERMS FG meetings
4. Stakeholders' meetings
5. Management Board meetings
6. HMA meetings
Topics
Activity
1. Periodic Safety Update Reports
1.1 Implementing measures (Reg. Art. 87a(f))
1.2 Business processes
1.3 SOP/WIN/Template/Guideline
Consultation
Finalisation
Adoption
Training
1.4 IT requirements
2. PASS/PAES
2.1 Implementing measures (Reg. Art. 87a(g))
2.2 Business processes
2.3 SOP/WIN/Template/Guideline
2.4 IT requirements
3. Product Information
3.1 Implementing measures (Reg. Art. 87a(c))
3.2 Business processes
3.3 SOP/WIN/Template/Guideline
3.4 IT requirements
4. EudraVigilance/Adverse Drug Reactions reporting
4.1 Implementing measures (Reg. Art. 87a(e))
4.2 Business processes
4.3 SOP/WIN/Template/Guideline
4.4 IT requirements
5. Committees
5.1 Business processes
5.2 Rules of procedure/Mandate
5.3 Committee membership
5.3 SOP/WIN/Template/Guideline
5.4 IT requirements
6. Referrals
6.1 Business processes
6.2 SOP/WIN/Template/Guideline
6.3 IT requirements
7. Fees* (specific planning foreseen)
8. Communication/Transparency
8.1 Business processes
8.2 Define common strategy
8.3 SOP/WIN/Template/Guideline
8.4 IT requirements
9. Literature Monitoring/Signal Detection
9.1 Implementing measures (Reg. Art. 87a(d))
9.2 Business processes
9.3 SOP/WIN/Template/Guideline
9.4 Outsourcing of literature monitoring
Award and sign contract
10. Inspections/Pharmacovigilance Systems
10.1 Implementing measures (Reg. Art. 87a(a-b))
10.2 Business processes
10.3 SOP/WIN/Template/Guideline
10.4 IT requirements
11. Risk Management Systems
11.1 Implementing measures (Reg. Art. 87a(f))
11.2 Business processes
11.3 SOP/WIN/Template/Guideline
11.4 IT requirements
12. Pharmacovigilance Audits
12.1 Business processes
12.2 Define common strategy
12.3 SOP/WIN/Template/Guideline
12.4 IT requirements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9.3 SOP/WIN/Template/Guideline
9.4 Outsourcing of literature monitoring
Monitor literature
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7. Annexes

Annex 1

Mandate for the EMA/MSs Project Teams and the Project Coordination Group

1. Purpose

This paper sets out the mandates for the EMA / MSs Project Teams and the Project Coordination Group for preparing for the implementation of the new pharmacovigilance legislation. The paper sets out the membership and chairmanship of the teams and the group, the deliverables for which the teams are responsible, the methodology for delivering and the timeframes for reporting to the Project Coordination Group and the Project Oversight Committee (the ERMS-FG).

2. Membership and Chairmanship

EMA / MSs Project Teams will have a membership made up of appointments from the Member States (nomination process through PhVWP, CHMP, CMD(h), and PhV IWG) and from EMA (made up of leaders from the EMA internal sub-project teams). Heads of Medicines Agencies will be invited to review the nominations made for their respective Member State. Each EMA / MSs Project team will be co-chaired by a Member State and an EMA Co-Chair. Each EMA / MSs Project team will be supported organisationally by the EMA secretariat and it should be noted that for content, the EMA / MSs Project Teams will also be supported by EMA internal sub-project teams.

The Project Coordination Group will be made up of the Co-Chairs of the EMA / MSs Project Teams and co-chaired by an EMA and a Member State Co-Chair (Dr Peter Arlett and Dr June Raine respectively). The Project Coordination Group will be supported by the EMA secretariat.

3. Responsibility for Deliverables

The EMA / MSs Project Teams shall be responsible for delivering:

- Technical drafts for legislative implementing measures
- Papers to support decisions where key strategic and policy orientations are needed for implementation
- Technical drafts for guidelines (which should normally be proceeded by draft concept papers when the timeframe for delivery allows)
- Peer-review of business requirements for IT systems impacting directly on the Member States
- Progress reports and deliverables to the Project Coordination Group

The Project Coordination Group shall:

- Track progress with implementation
- Coordinate the development of deliverables and ensure coherent allocation of tasks between the Project Teams
- Ensure coherence between and within legislative implementing measures and Good Vigilance Practices
- Ensure that deliverables are provided to the Project Oversight Committee and that key scientific and technical fora have been consulted, where appropriate
- Ensure that risks of non-delivery or delayed-delivery are reported to the Project Oversight Committee with proposals for remedial action where necessary

4. Methodology and Timelines

Within the EMA / MSs Project Teams:

- The Co-Chairs shall ensure that each deliverable has an individual clearly named for delivery (Topic Lead or Rapporteur). For some deliverables a second individual ('Co-Rapporteur') will be named and this will likely be to allow the EMA and Member State implementation issues to be considered, where appropriate.
- For each deliverable a timeframe with milestones shall be agreed and recorded by the Co-Chairs. The EMA / MSs Project Teams shall meet at least monthly either face to face or via teleconference.
- The Co-Chairs shall report progress and supply deliverables to the Project Coordination Group by 12.00 GMT on the Friday before the Project Coordination Group meeting.
- The EMA Co-Chair shall be responsible for feeding back to the EMA internal sub-project teams.

The Project Coordination Group shall:

- Meet at least monthly either face to face or via teleconference and this meeting shall take place during the week of CHMP/PhVWP/CMD(h).
- The Project Coordination Group shall provide a written report to each the Project Oversight Committee.