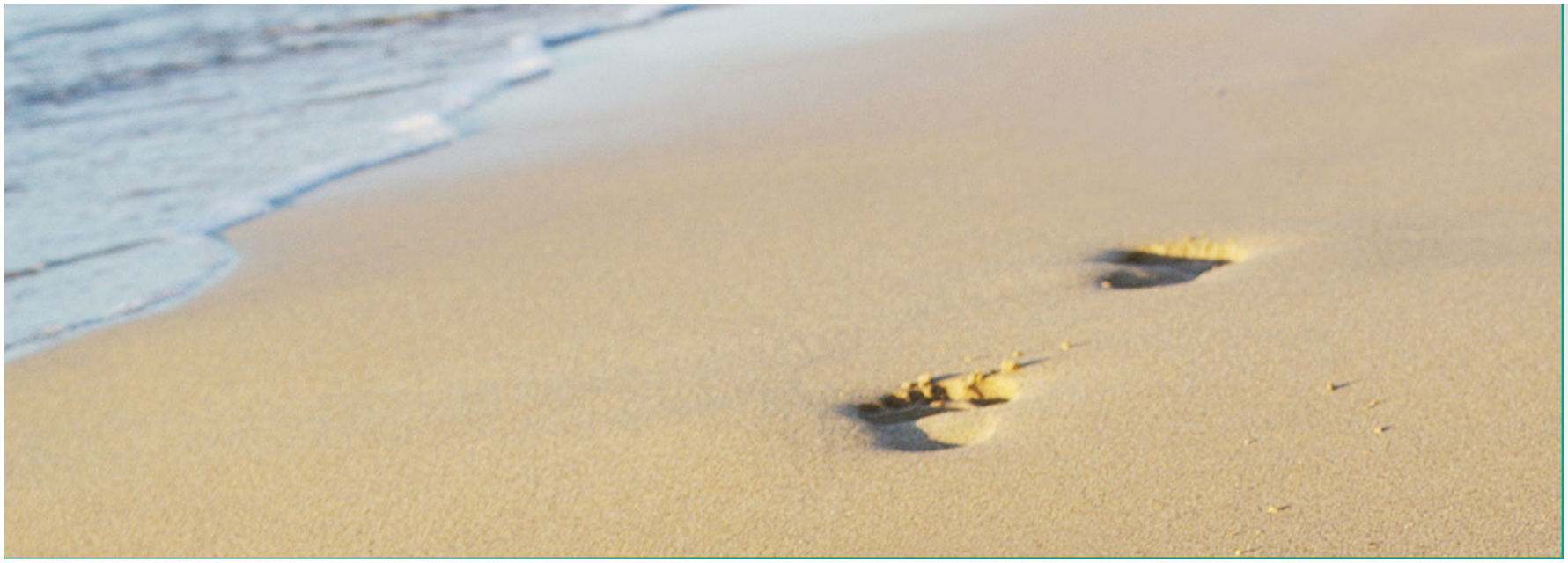


Recent developments in Pharmacovigilance from the Regulator's Perspective

In strategy, competence, quality and flexibility

Yes Leading in Regulatory Solutions



- Pharmacovigilance
- Regulatory Affairs Operations
- Medical Writing & toxicology

Recent developments in Pharmacovigilance

The introduction of new PV legislation in July 2012 is the biggest change to the regulation of human medicines in the European Union (EU) since 1995.

Similarly, the United States Food and Drug Administration (USFDA) has become more open to inclusion of non-safety data collection in its safety surveillance mandates and more proactive risk management approach.



Recent developments in Pharmacovigilance

Trends-

1. To strengthen the instruments of protection of human health-

- Continuous monitoring of the risk-benefit ratio of drugs
- Greater transparency
- Power to penalize producers for the failure to meet Pharmacovigilance obligations

2. Partial harmonization of the different Pharmacovigilance systems



Recent developments in Pharmacovigilance

New definition of adverse drug reaction:

- An adverse drug reaction is a response to a medicinal product which is noxious and unintended.
- Also covers
  - Medicinal errors
  - The use outside the terms of the marketing authorization,
    - Overdose
    - off-label use
    - Misuse
    - Abuse
    - occupational exposure



Recent developments in Pharmacovigilance

Volume 9 a?



The key to the success of the legislation is the Good Pharmacovigilance Practice (GVP) document which replaced Volume 9A.

Main Pillars

1. The new Good Vigilance Practice Guidelines (GVP)
2. The Pharmacovigilance Risk Assessment Committee (PRAC)
3. The Pharmacovigilance System Master File (PSMF)
4. Using a Periodic Benefit Risk Evaluation Report (PBRER)
5. More stringent ICSR submission rules
6. Publishing summaries of Risk Management Plans (RMP)
7. Requirement to perform Post-Approval Safety Studies (PASS)
8. Assignment of an Additional Monitoring Status
9. Commitment to openness and transparency
10. EudraVigilance policy to disclose postmarketing safety information to the Public



Risk Management



RMP

- In accordance to new legislation, RMP should be risk proportionate and needs to be submitted for all new products.
- Educational materials for HCPs and patients are required in RMP for a new product.
- The authorized products require RMP if there are issues affecting the risk benefit balance.
- Summaries of RMPs shall be made public publicly available via web portals.

Risk Management

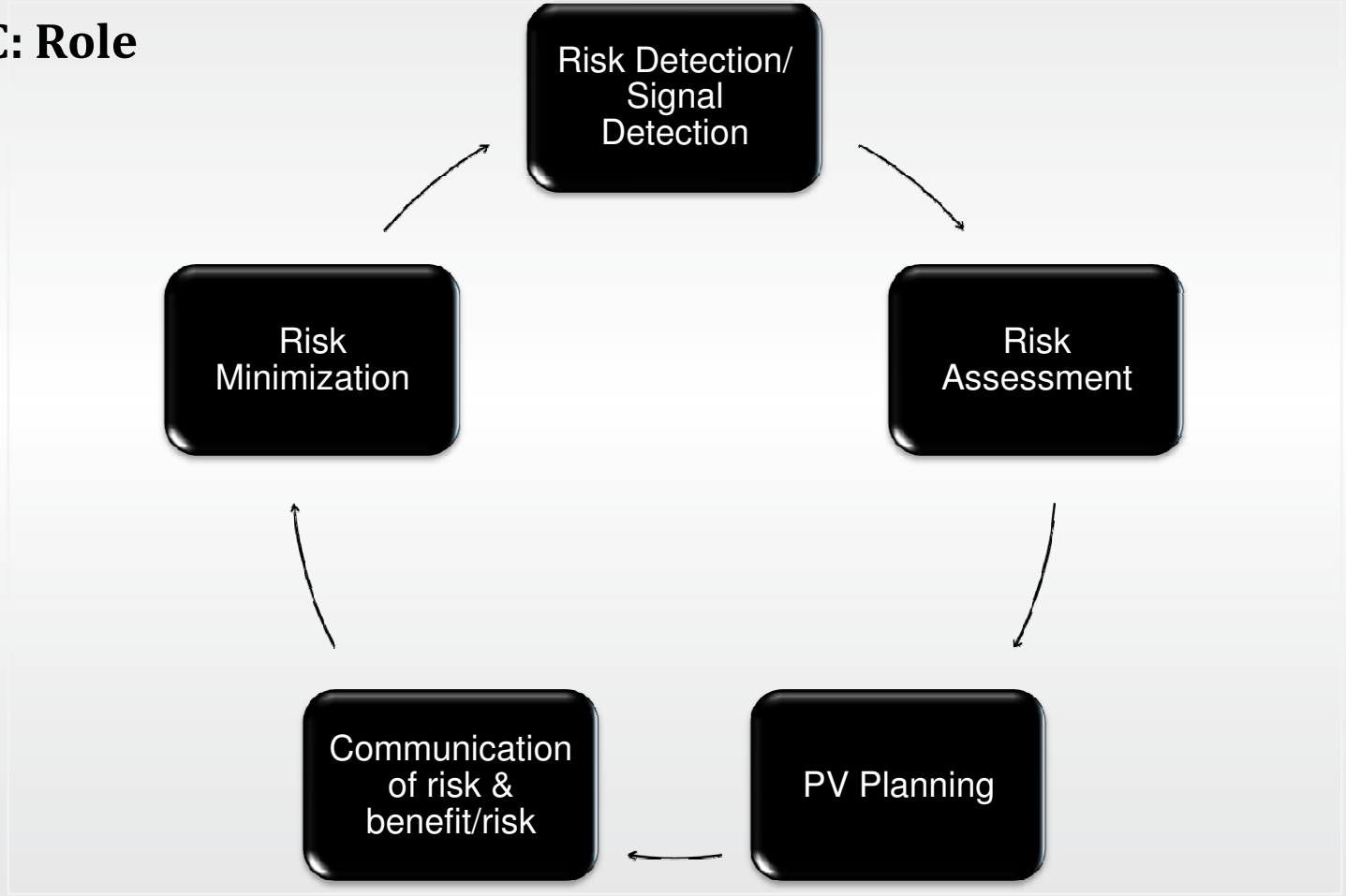
PRAC

- PRAC is a new scientific committee within the EMA, created to ensure access to the best scientific and medicinal expertise for the evaluation of the safety of medicines and risk minimization measures, with the ultimate goal of reducing ADRs.
- Will have regulatory oversight of RMPs



Risk Management

PRAC: Role



Risk Management

Risk Evaluation and Mitigation Strategies (REMS)

- The USFDA has obligation for manufacturers to implement special risk management programs, called REMS.
- If the benefits of drug outweigh the risks, then the applicant having an approved application for new drug or abbreviated new drug or biological medicinal product has to submit REMS. The proposed REMS must be submitted within 120 days of the USFDA notification for the protection of public health.



PV system Master File (PSMF)

As per the new legislation, Detailed Description of Pharmacovigilance System (DDPS) will no longer be required and is replaced by PSMF. MA applicants and MAHs are required to maintain PSMF.

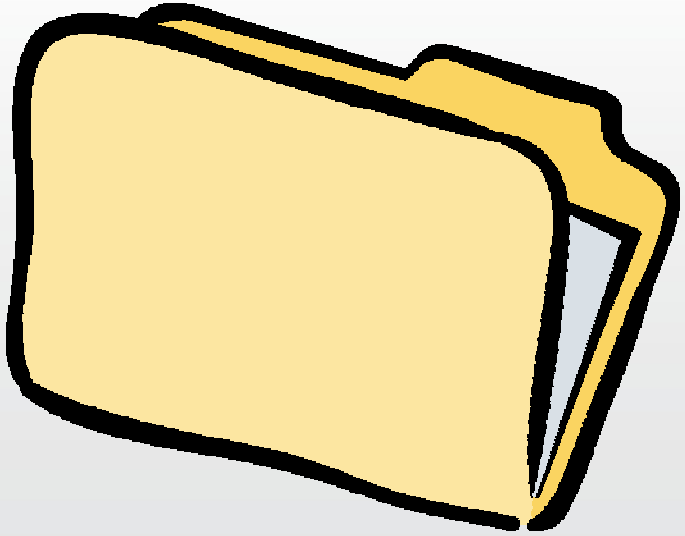
On request, the PSMF should be provided within seven days to CAs. The annexes of the PSMF contain comprehensive data demonstrating the current state of the PV system, including

- An overview of all marketing authorisations covered by the PSMF together with information on presence on the market (also outside EU) and specific safety monitoring requirements



PV system Master File (PSMF)

- Results of the current performance assessment [e.g. timeliness of Individual Case Safety Reports (ICSRs) reporting and PSUR submission, safety variations and adherence to RMP requirements]
- An audit schedule and critical findings from previous PV audits
- A detailed overview on the company's written procedures



Periodic Reporting

- In EU, PSUR is replaced with Periodic Benefit Risk Evaluation Report (PBRER).
- The PBRER does not work anymore as a detailed listing of ICSRs.
- The submission of periodic reports is also exempted for MAHs of generic, well-established used, homeopathic or traditional-use herbal medicinal products.
- Six monthly reports, summary bridging reports, or addendum reports will not be accepted.
- New assessment procedure involving PRAC
- Assessment reports of PSURs will be published on EMA web portal.



xEVMPD

- The Medicinal Product Dictionary has actually been in existence since 2005
- All MA Holders have been able to submit basic details of their products to the EMA
- Was not mandatory, so consequently the EVMPD contains less than 25% of the estimated 528,000 products authorized for use in the EU, and the data that is there is likely to be out of date.

xEVMPD

- The original legislation was amended in December 2010

…..the EMA shall set up a list of all medicinal products for human use authorized in the EU, and that marketing authorization holders were required, by 2 July 2012 at the latest, to electronically submit to the EMA information on all medicinal products for human use authorized or registered in the EU using the format defined by the EMA, and keep it up to date thereafter….

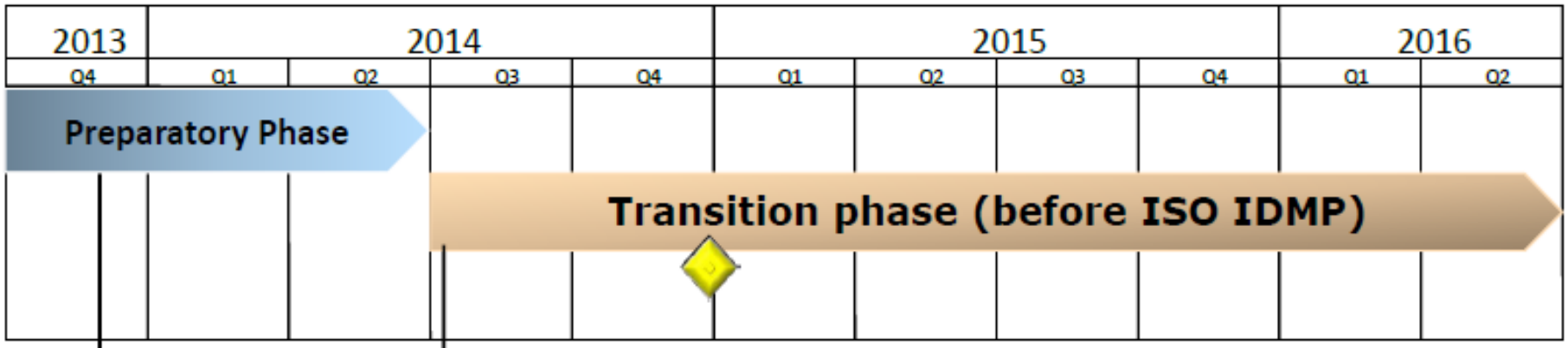
xEVMPD

Phased approach



- Initial submission phase: July 2011 - January 2014
- Transition maintenance phase: February 2014 – 2016
  - February 2014 - June 2014 (preparatory phase)
  - June 2014 onwards (Transition phase)

xEVMPD



December 2013 – June 2014

The aim is:

- For the Agency to upgrade the Agency's data entry tool and provide necessary guidance to support the maintenance submission
- For industry to start upgrading in-house IT systems

June 2014 – December 2014

The objective is to enable the MAHs to update, complete, improve the quality and submit the Article 57 data via the simplified process **before the end of 2014**.

From January 2015

MAHs to continue notifying any changes affecting the Article 57 data by means of the simplified process within **30 calendar days** from the date of which the changes have been authorised.

Partial harmonization of the different Pharmacovigilance systems

Simplify the sponsors' activities and
increase the efficacy of pharmacovigilance

The ICH of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) has elaborated a pharmacovigilance guideline for medicines approved in the U.S., the E.U. and Japan

Pharmacovigilance relevant sections of Module 1 of CTD

MedDRA

Thank You


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