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Developing Countries Vaccine Manufacturers Network

Vaccine Safety Monitoring
DCVMN Regional Training Workshop
Sao Paulo 27 - 30 May 2019

Risk Management: An Industry Perspective

Pharmacovigilance Planning

Risk Minimization Measures

Safety Communication

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What does Safety imply?

In everyday terms:

Safety defined as exemption from injury or loss, freedom from danger, state of not being liable to danger or injury.

Source: Webster's New World Dictionary of the American Language

(1979, Simon & Schuster, New York, NY)

FDA Definition of Safety:

Safety means the relative freedom from harmful effect to persons affected directly or indirectly, by a product when prudently administered.

Harm: Physical or material injury; hurt; damage

What does Risk imply?

In everyday terms:

Risk as the chance of injury, damage, or loss. Therefore, to put oneself “at risk” means to participate either voluntarily or involuntarily in an activity or activities that could lead to injury, damage, or loss.

Source: Webster's New World Dictionary of the American Language (1979, Simon & Schuster, New York, NY)

In statistical and epidemiological terms:

Risk is an expression of probability, usually (but not invariably) the probability of an adverse event, such as disease, injury, or death; i.e., risk can be quantified:

- Absolute risk: magnitude of the disease risk in a group of people with specific exposure
- Relative risk: strength of association between an exposure and a disease
- Attributable risk: proportion of disease risk that can be attributed to an exposure

Safety / Risk

Safety: Acceptance of risk - a personal / societal decision

Risk: Probability of occurrence of an adverse event for an individual within a specified time

Safety assessment is

assessment of the benefit / risk balance

EU Legislation: GVP Annex I Definitions Dec 2012:

Risk-Benefit Balance: An evaluation of the positive therapeutic effects of the medicinal product in relation to the risks [DIR 2001/83/EC Art 1(28a)], i.e. any risk relating to the quality, safety or efficacy of the medicinal product as regards patients' health or public health [DIR 2001/83/EC Art 1(28)].

Safety: Balance of Benefit and Risk

BENEFITS:

Prevention of disease

Herd immunity

....

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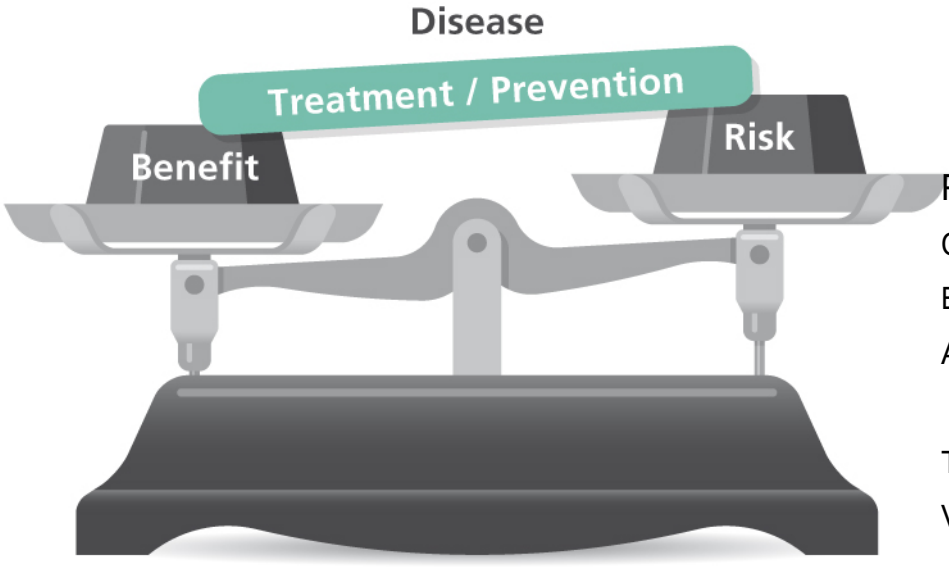


RISKS:

Guillain Barre syndrome

Encephalopathy

ADEM (acute disseminated encephalomyelitis)

Thrombocytopenia

Vasculitis

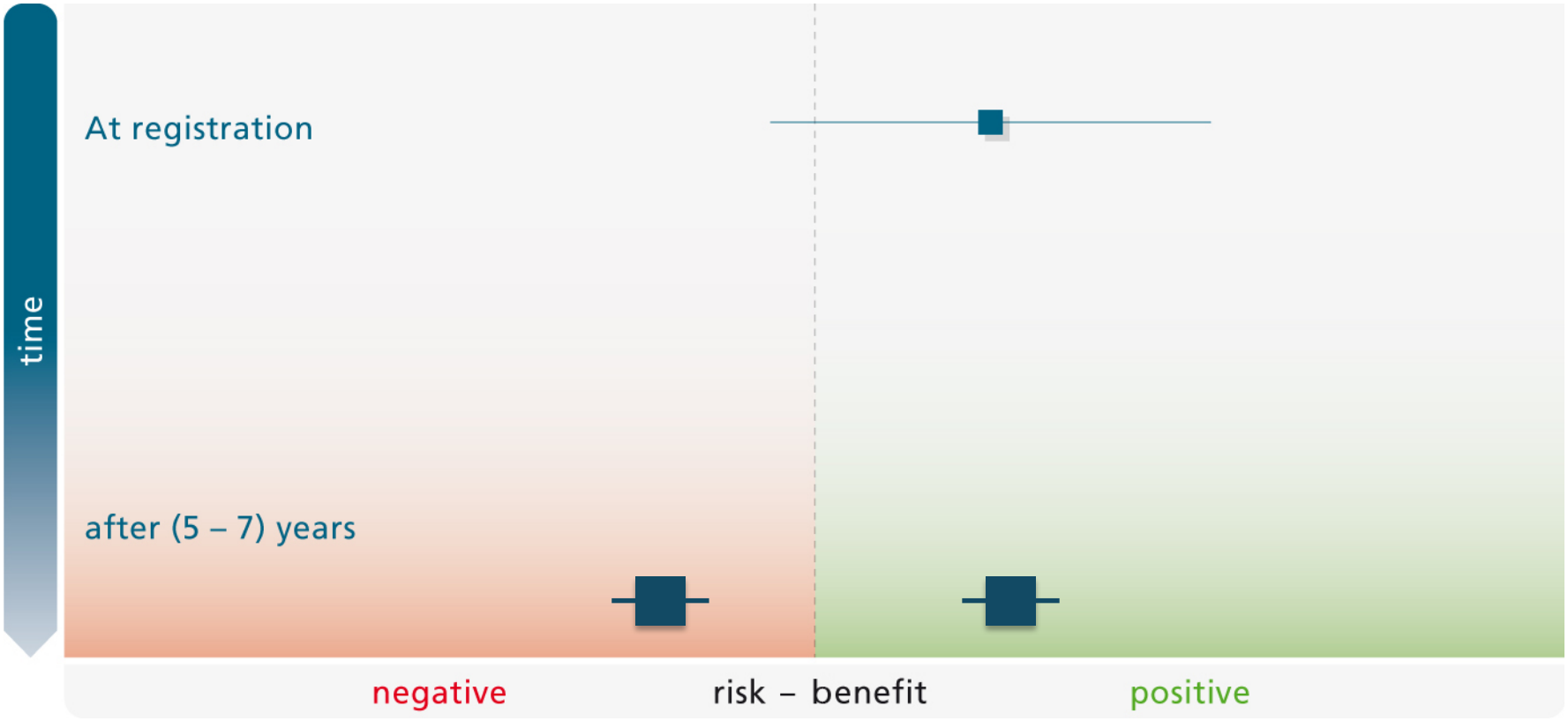
....

....

Risk Profile: usually measured in clinical trials with one more of the following:

- Adverse Events / Determination of clinical signs and symptoms
- Physical examination (e.g., vital signs, neurological, ophthalmologic, general physical)
- Laboratory evaluations of biological samples (e.g. hematology, clinical chemistry, urinalysis)
- Special tests and procedures
- Psychiatric tests and evaluations
- Other test depending on the indication

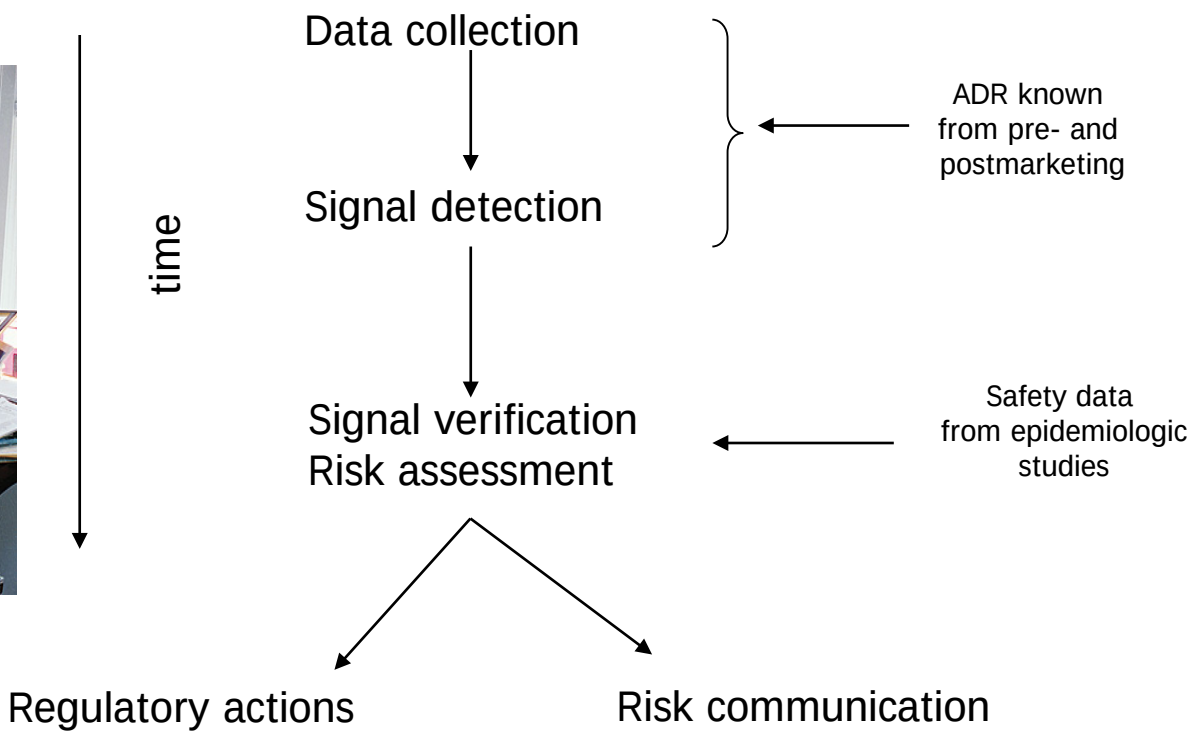
Benefit – Risk Evaluation



Benefit – Risk evaluation is a continuous task during the whole lifespan of a medicinal product and should be presented

- in a structured manner
- with clear explanation of the methodology and reasoning used
- with clear assumptions, considerations and judgment or weighting that support the conclusions

Risk Management – old concept
Reactive Pharmacovigilance



ICH E2E Pharmacovigilance Planning - Risk Management

... the overall and continuing process of minimizing risks throughout a product's lifecycle to optimize its benefit/risk balance.

"...shall comprise a set of pharmacovigilance activities and interventions designed tom identify, characterise, prevent or minimise risks relating to medicinal products, including the assessment of the effectiveness of those interventions."

INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED TRIPARTITE GUIDELINE

PHARMACOVIGILANCE PLANNING
E2E

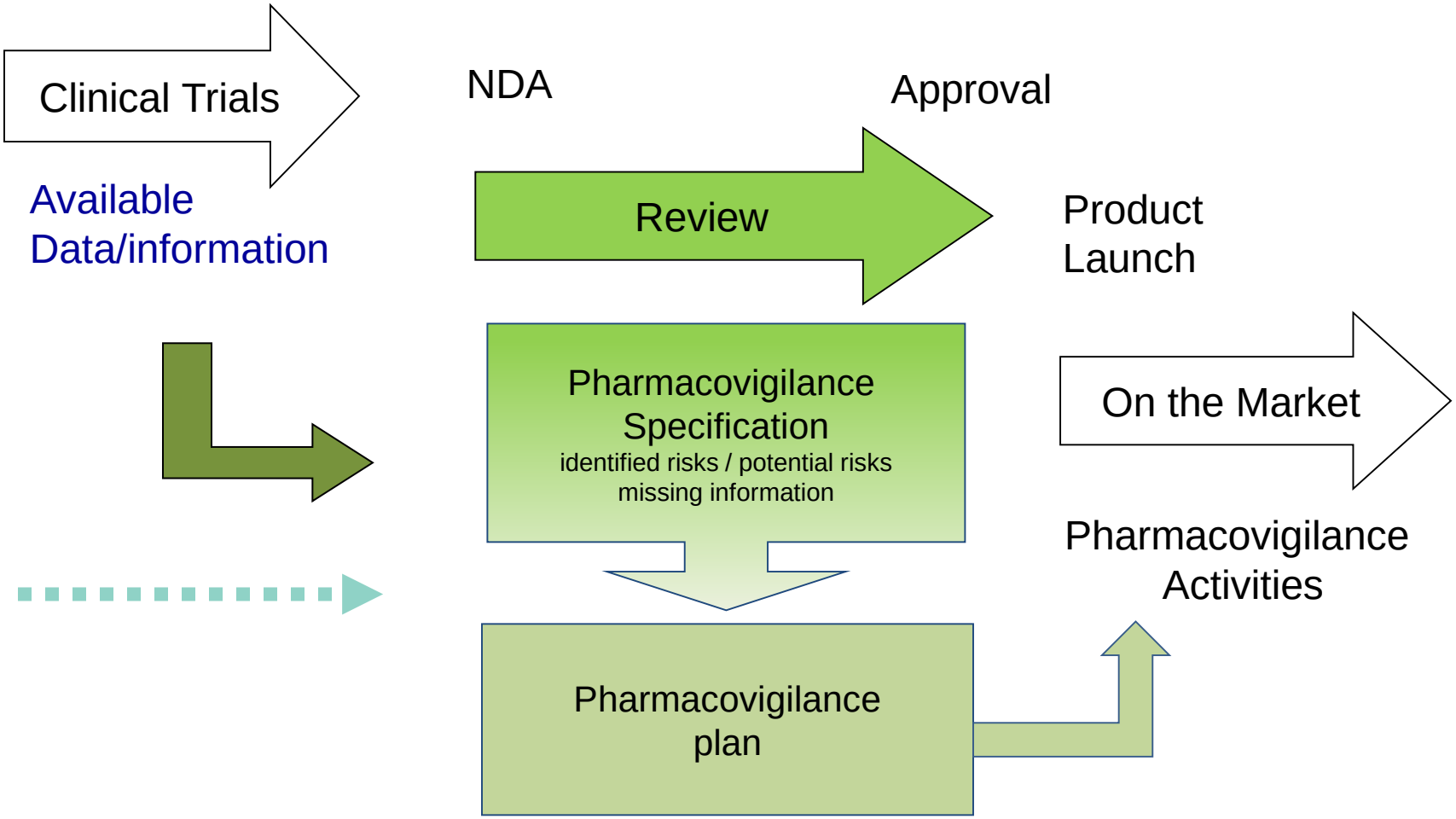
Current *Step 4* version
dated 18 November 2004

Risk Management
ICH E2E Pharmacovigilance Planning

- The "**E2E: Pharmacovigilance Planning**" guideline is intended to aid industry and regulators in planning of pharmacovigilance activities, especially in preparation for the early post-marketing period of a new drug.
- The guideline describes a method for documenting risks and proposes a structure for a pharmacovigilance plan.
- The guideline does not describe other methods to reduce risks from drugs, such as risk communication.

FDA and EMA adopted ICH E2E in 2005

Concept of the ICH E2E Guideline



Risk Management System

Risk Management is the overall and continuing process of minimizing risks throughout a product's lifecycle to optimize its benefit/risk balance:

Guideline on Risk Management Systems for Medicinal Products for Human Use (EMA / CHMP/96268/2005)

EU Good Vigilance Practice, Module V: A set of pharmacovigilance activities and interventions designed to identify, characterize, prevent or minimize risks relating to a medicinal product, including the assessment of the effectiveness of those interventions (Annex V, ICH E2C(R2) Guideline).

Global Risk Management Planning
The Challenge of Reconciling the Differences

FDA: Risk assessment and risk minimization form what FDA calls *risk management*. Risk Management is an iterative process of

(1) assessing a product's benefit-risk balance,

(2) developing and implementing tools to minimize its risks while preserving its benefits,

(3) evaluating tool effectiveness and reassessing the benefit-risk balance,

(4) making adjustments, as appropriate, to the risk minimization tools to further improve the benefit-risk balance

Risk Evaluation and Mitigation Strategies REMS

Europe: A set of pharmacovigilance activities and interventions designed to identify, characterize, prevent or minimize risks relating to medicinal products, including the assessment of the effectiveness of those interventions

GVP Module V and Module XVI

Risk Management in the EU
GVP Module V and GVP Module XVI

28 March 2017
EMA/838713/2011 Rev 2*

Guideline on good pharmacovigilance practices (GVP)
Module V – Risk management systems (Rev 2)

Date for coming into effect of first version	2 July 2012
Date for coming into effect of Revision 1	28 April 2014
Draft Revision 2* finalised by the Agency in collaboration with Member States	16 February 2016
Draft Revision 2 agreed by the European Risk Management Facilitation Group (ERMS FG)	23 February 2016
Draft Revision 2 adopted by Executive Director	24 February 2016
Release for public consultation	29 February 2016
End of consultation (deadline for comments)	31 May 2016
Revised draft Revision 2 finalised by the Agency in collaboration with Member States	9 March 2017
Revised draft Revision 2 agreed by the EU Network Pharmacovigilance Oversight Group (EU-POG)	23 March 2017
Revised draft Revision 2 adopted by Executive Director as final	28 March 2017
Date for coming into effect of Revision 2*	31 March 2017

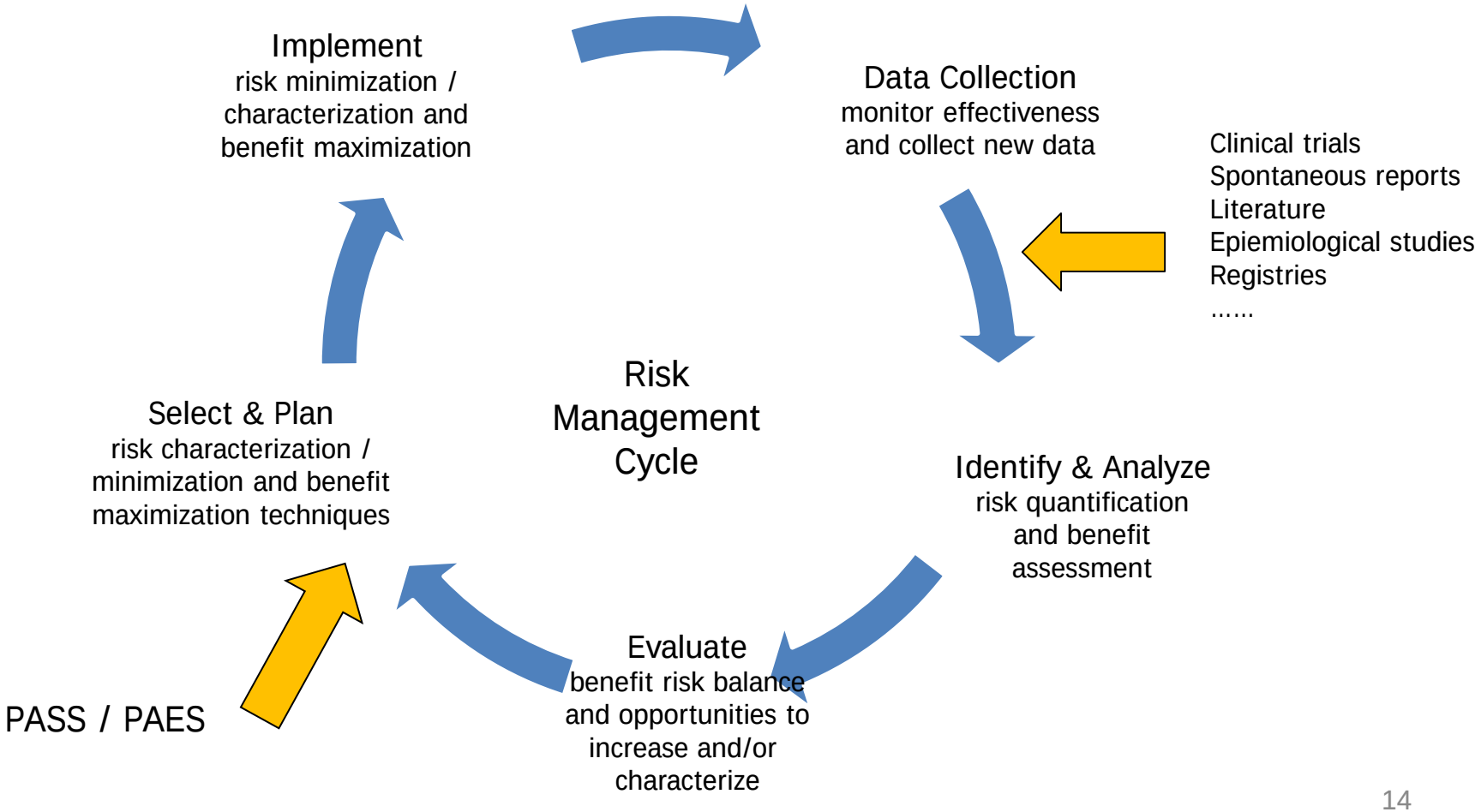
28 March 2017
EMA/204715/2012 Rev 2*

Guideline on good pharmacovigilance practices (GVP)
Module XVI – Risk minimisation measures: selection of tools and effectiveness indicators (Rev 2)

Date for coming into effect of first version	1 March 2014
Date for coming into effect of Revision 1	28 April 2014
Draft Revision 2* finalised by the Agency in collaboration with Member States	6 March 2017
Draft agreed by the EU Network Pharmacovigilance Oversight Group (EU-POG)	23 March 2017
Draft adopted by Executive Director as final	28 March 2017
Date for coming into effect of Revision 2*	31 March 2017

Risk Management – new concept
GVP Module V

From Risk Management to
Benefit – Risk Management



Risk Management System (RMS)
Definition GVP Module V.B.1

‘ a set of pharmacovigilance activities and interventions designed to identify, characterize, prevent or minimizse risks relating to a medicinal product, including the assessment of the effectiveness of those activities and interventions’. [DIR 1(28b)]

Principles of Risk Management
GVP Module V.B.2

- The overall aim of risk management is to ensure that the benefits exceed the risks by the greatest achievable margin for the individual patient and for the target population as a whole
- Single risk evaluation comprizes: risk identification, risk assessment, risk minimization and risk communication
- Multiple risk evaluation – risk management
  - Characterization of the safety profile including missing information
  - PV activities to further monitor the safety profile and adapt characterization
  - Risk minimizing measures and assessment of their effectiveness

Responsibilities for Risk Management within Industry

Marketing Authorization Holder / Applicant:

- Constantly monitoring product risks according to relevant legislation including reporting of the results to Competent Authority, as required
- Taking appropriate risk minimizing / benefit maximizing measures including active updates and prompt communication of new information; ensuring accuracy of this information
- Taking responsibility for the content and accuracy of the RMP by ensuring oversight by someone with appropriate scientific background
- Expectation:
  - RMP primarily considered a PV document
  - RMP to be managed by personnel with appropriate PV training (e.g., PV or RA Department)

Risk Management

Risk Management =

Risk Identification + Risk Assessment + Risk Minimization + Risk Communication

EU: In addition, Assessment of the impact of pharmacovigilance activities

Risk Management is a complex process which need governance structure.

Safety Management Teams (SMTs) are an operating model to ensure product safety and to document continuous and permanent safety evaluation of a medicinal product.

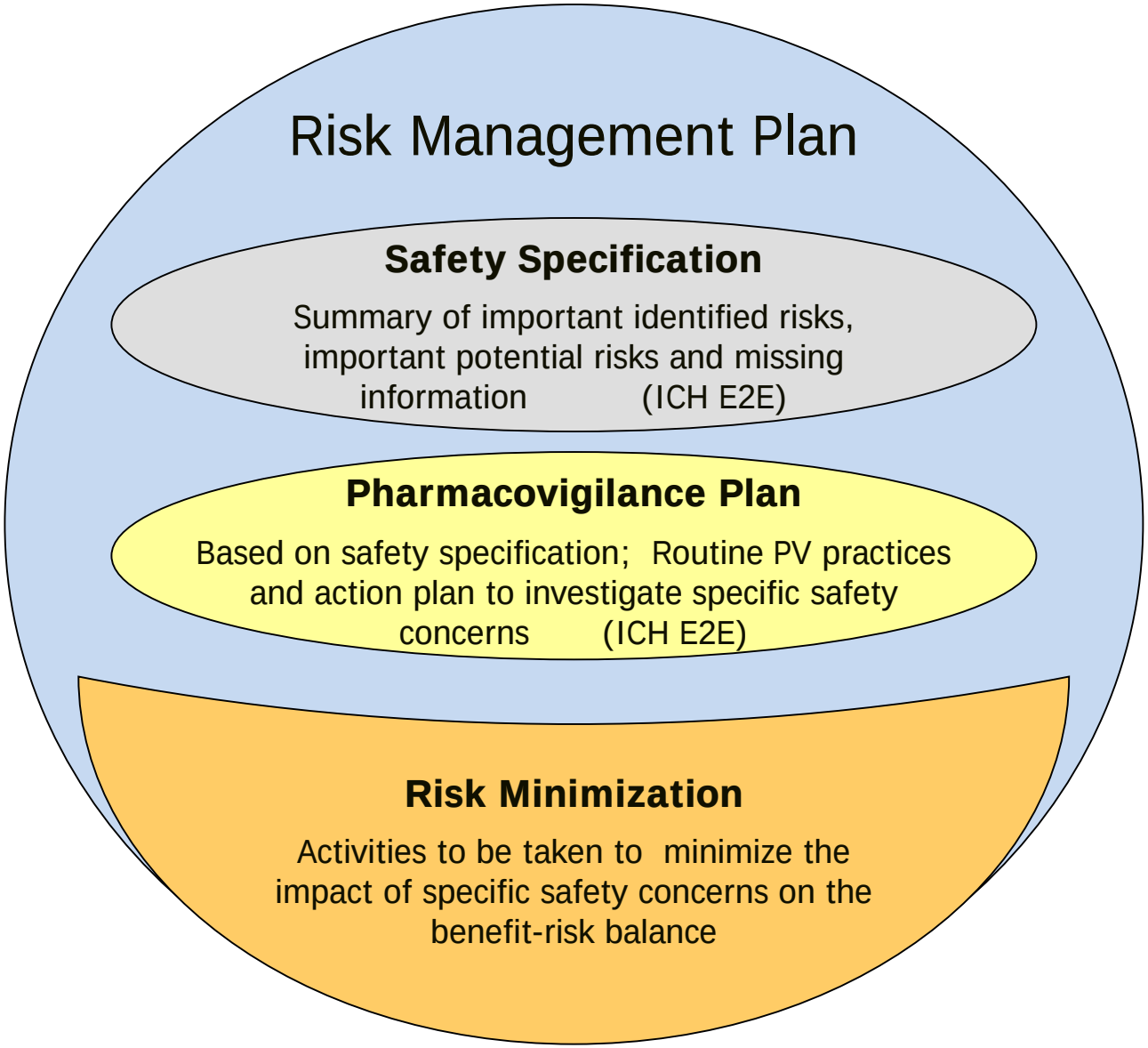
Risk Management Plan (RMP)

" a detailed description of the risk management system." (DIR 2001/83/EC Art1 (28c))

- identify or characterise the safety profile of the medicinal product(s) concerned,
- indicate how to characterise further the safety profile
- document measures to prevent or minimise the risks associated
  - including assessment of effectiveness of the interventions
- document post-authorisation obligations that have been imposed as a condition of MA
- implicit requirements:
  - describe what is known about the safety profile
  - Indicate level of certainty that efficacy shown in clinical trials is seen in everyday practice
  - Include how effectiveness of risk minimisation measures will be assessed

Risks need to be understood in the context of benefit

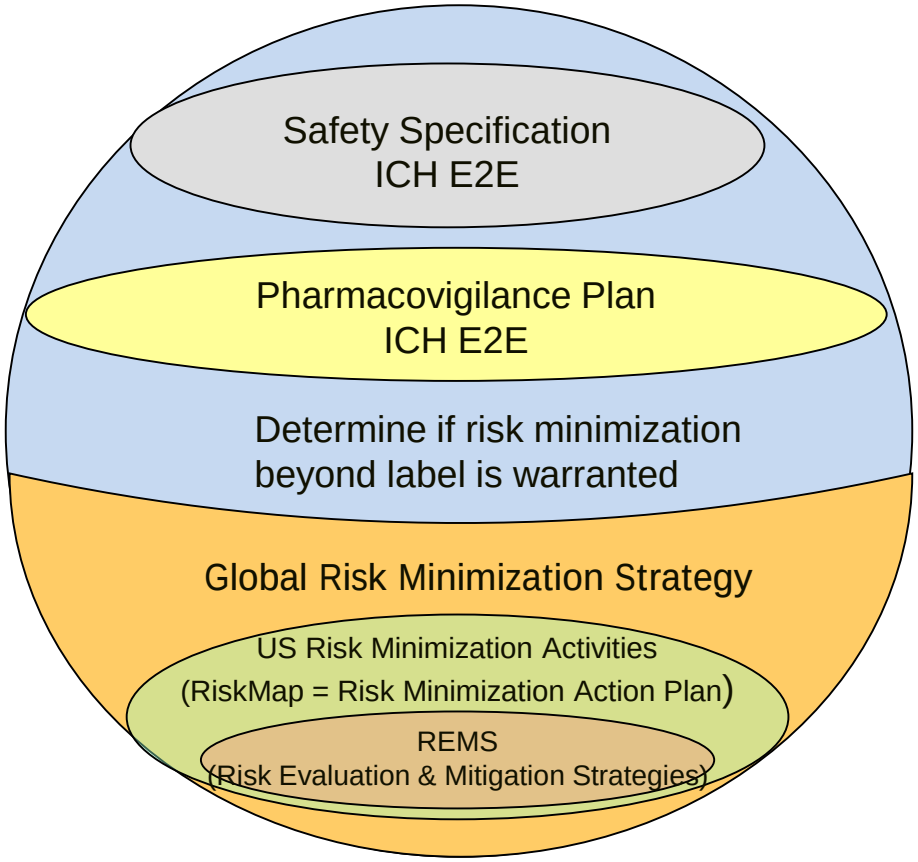
Components of a Risk Management Plan



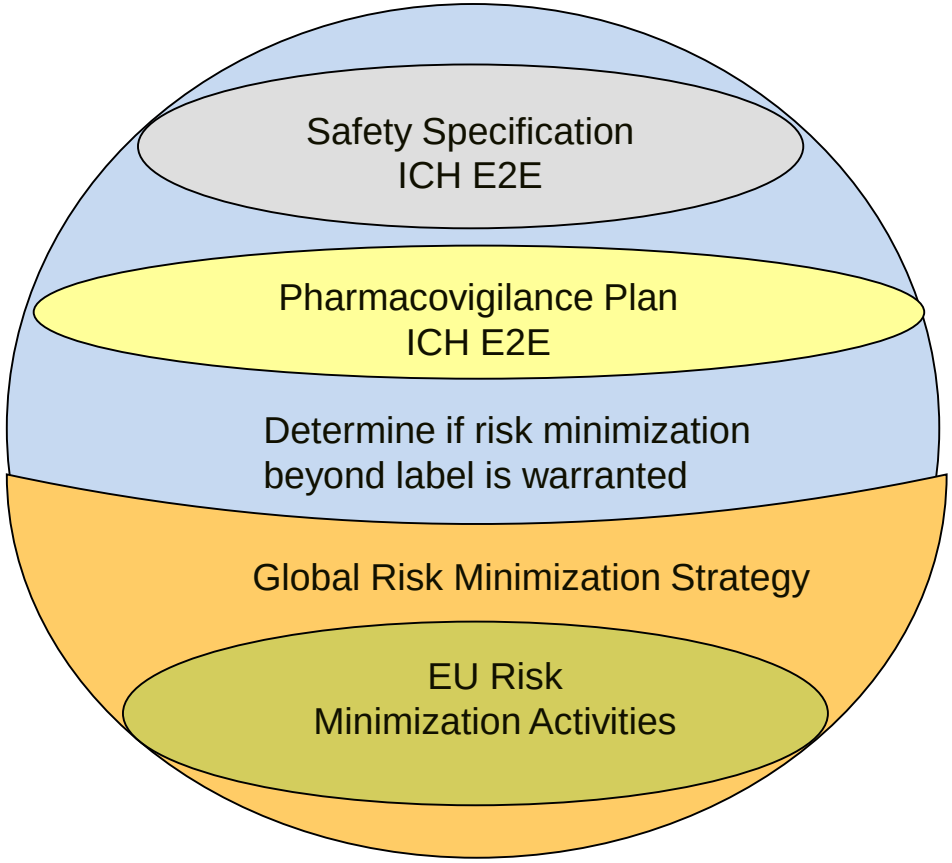
Simmons, 2012

Global RMP – US / EU RMP Relationship

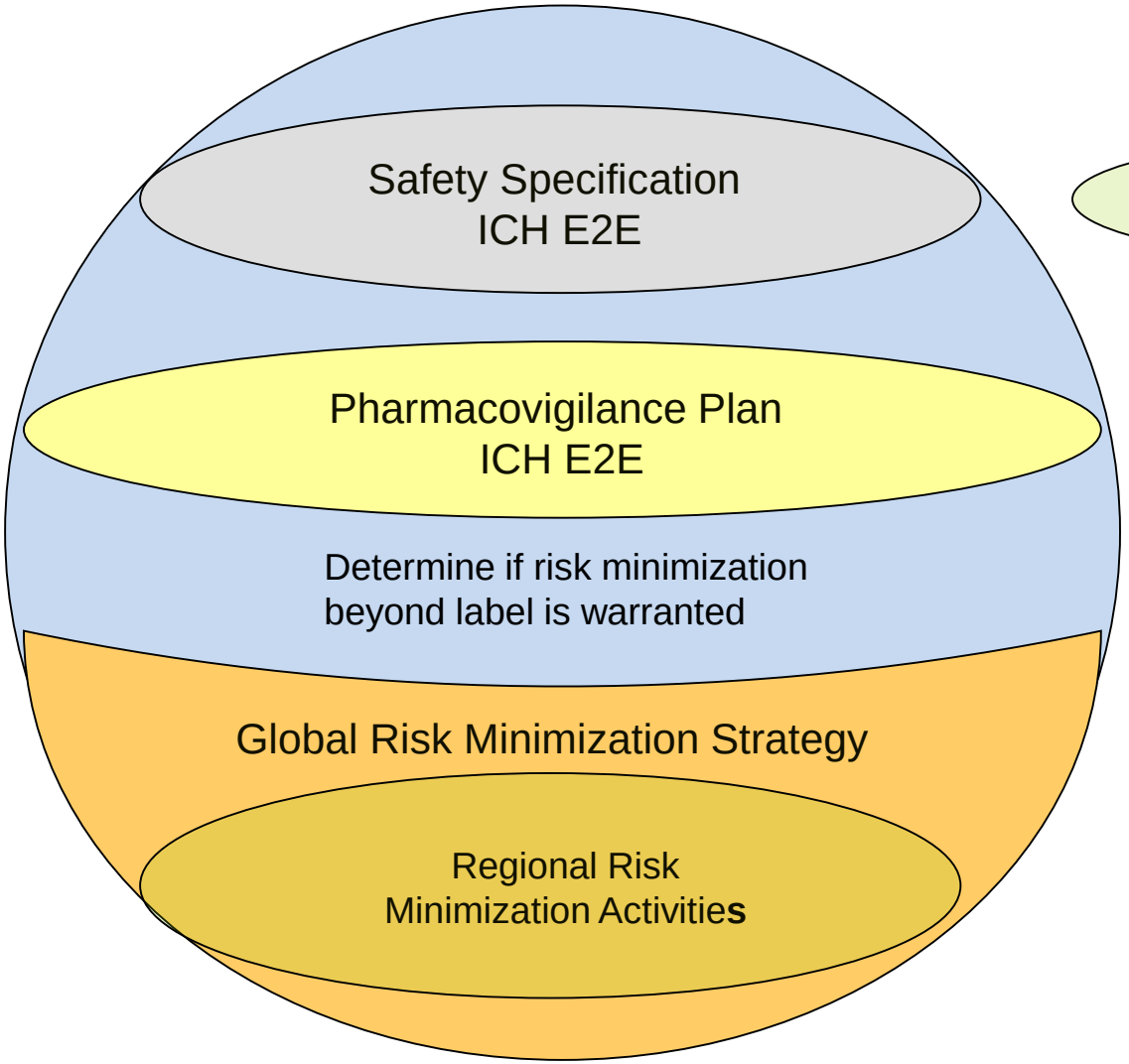
US RMP Relationship



EU RMP Relationship



Regional Variations of Global RMP



Regional Safety Specification Req

Regional PV Requirements

EU Risk Management Plan (RMP)
GVP Module V Template

Part I Product Overview

Part II Safety Specification

- Module SI: Epidemiology of the indications(s) and target populations(s)
- Module SII: Non-clinical part of the Safety Specification
- Module SIII: Clinical trial exposure
- Module SIV: Populations not studied in clinical trials
- Module SV: Post authorisation experience
- Module SVI: Identified and potential risks
- Module SVII: Additional EU requirements for Safety Specification
- Module SVIII: Summary of Safety Concerns

Part III Pharmacovigilance Plan

Part IV Plans for studies on effectiveness and long term efficacy

Part V Risk Management Plan(s)

Part VI Summary of Activities in the EU-BRMP

Part VII Annexes

EU: Risk Management System – Vaccines
GVP P1

- GPV P I supplements GVP Module V and presents vaccine-specific aspects of the Risk Management Plan (RMP) – in red vaccine-specific additions made in GPV P I :

Part I **Product Overview**

Part II Safety Specification

Module SI: Epidemiology of the indications(s) and target populations(s)

Module SII: Non-clinical part of the safety specification

Module SIII: Clinical trial exposure

Module SIV: Populations not studied in clinical trials

Module SV: Post authorisation experience

Module SVI: Additional EU requirements for safety specification

Module SVII: Identified and potential risks

Module SVIII: Summary of safety concerns

Part III Pharmacovigilance Plan: **Routine PV activities, Additional PV activities**

Part IV **Plans for post-authorisation efficacy studies**

Part V **Risk minimisation measures**

Part VI Summary of activities in the risk management plan by medicinal product (EU-BRMP)

Part VII Annexes to the risk management plan

Stand-alone RMP summary
GVP Module V.B.12.1.

- Overview of disease epidemiology
- Summary of the existing efficacy data
- Summary of main safety concerns (identified, potential and missing information)
- Summary of risk minimization measures by safety concern (routine and additional)
- Planned post-authorization (safety and efficacy) development plan
- Studies, which are a condition of the marketing authorization
- Major changes to the RMP over time

Written in "lay language" and with links to Product Information

Risk Management Planning /1
Practical Considerations

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When to start RM Planning – CIOMS VI* Principles

- Early in development; based on non clinical data & information on closely related compounds
- Establish a procedure & Multi Disciplinary Team (e.g., Safety Management Team SMT) and advisory bodies
- Determine background data
- Ready accessibility of all safety data
- Develop a proactive approach
- Establish time frames and milestones
- Decision making: focus on safety reviews

* Management of Safety Information from Clinical Trials 2005

Risk Management Planning /2
Practical Considerations

The Role of Epidemiology

- Important early in development and throughout the RM process
- Critical for the Safety Specification and PV Plan……bridging the knowledge gap
  - Defines demographics & expected characteristics of the target population
    - co morbidities
    - anticipated AEFI profile in usual clinical practice
  - Design of post marketing safety studies / registries
  - Identification of existing databases
  - Assess effectiveness of risk minimization measures

Risk Management Planning /3
Practical Considerations

What format to use

- European template now in use since October 2006, new revised version 2 October 2018 - why reinvent the wheel?
- Aim for a globalized document; concept of a “Core RMP” based on ICH E2E and the European template with adaptation as required to meet local needs
- Getting the safety specification right is critical
- Use tabulations and graphical presentation of data
- Strategic risk minimization plan should be the same globally; implementation can be tailored to local medical practice
- Regulatory feedback and early discussion are useful to optimize content

Preparation of the RMP
Responsibilities

- The preparation is a highly collaborative exercise
- Project lead is within PV with roles and responsibilities of the different contributors / stakeholders clearly defined
- RMP preparation should be coordinated with preparation of other submissions
- The modular structure used to facilitate
  - Tailored modules per product and MAA type
  - Updates per module
  - Core RMPs and additional regional RMPs
  - Exchangeable modules with PSUR

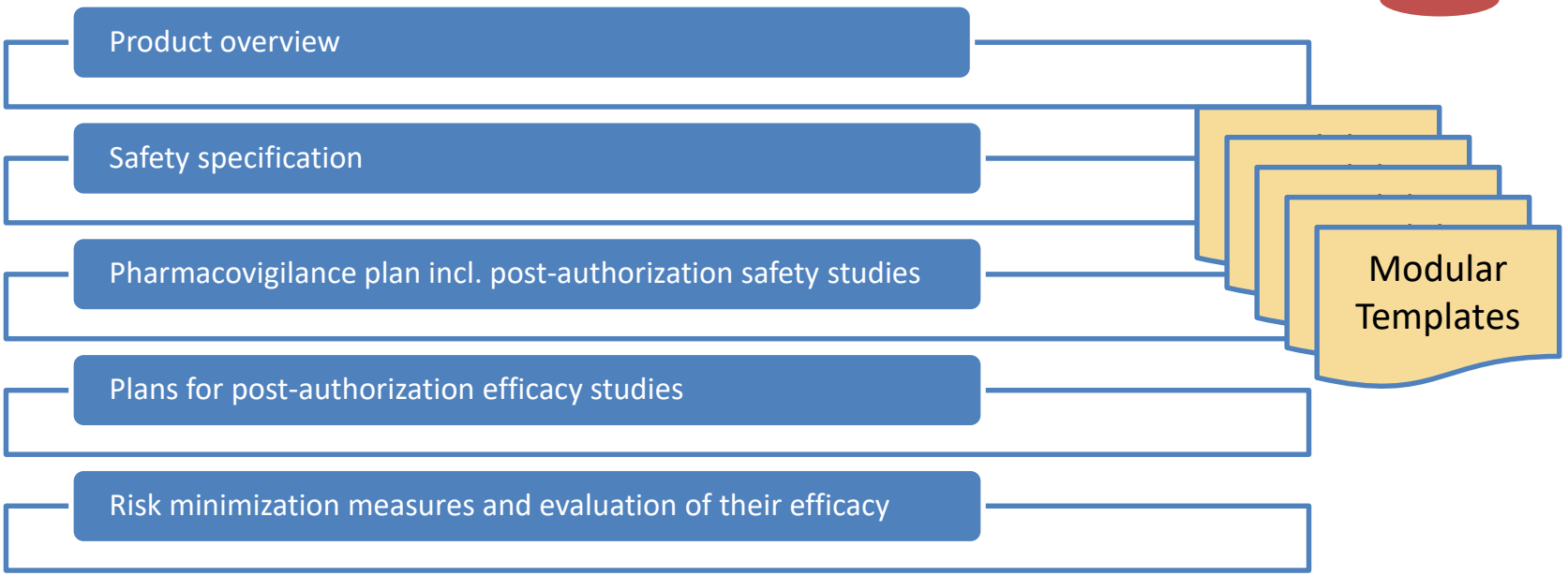
Preparation of RMP:
Regulatory guidance and structure

Core RMP follows EU requirements

- GVP (Good Pharmacovigilance Practice) Module V
- GVP P1: Product- or Population-Specific Considerations I: Vaccines

GVP Module V

GVP P1 Vaccines



Preparation of RMP: Cross-functional work sharing

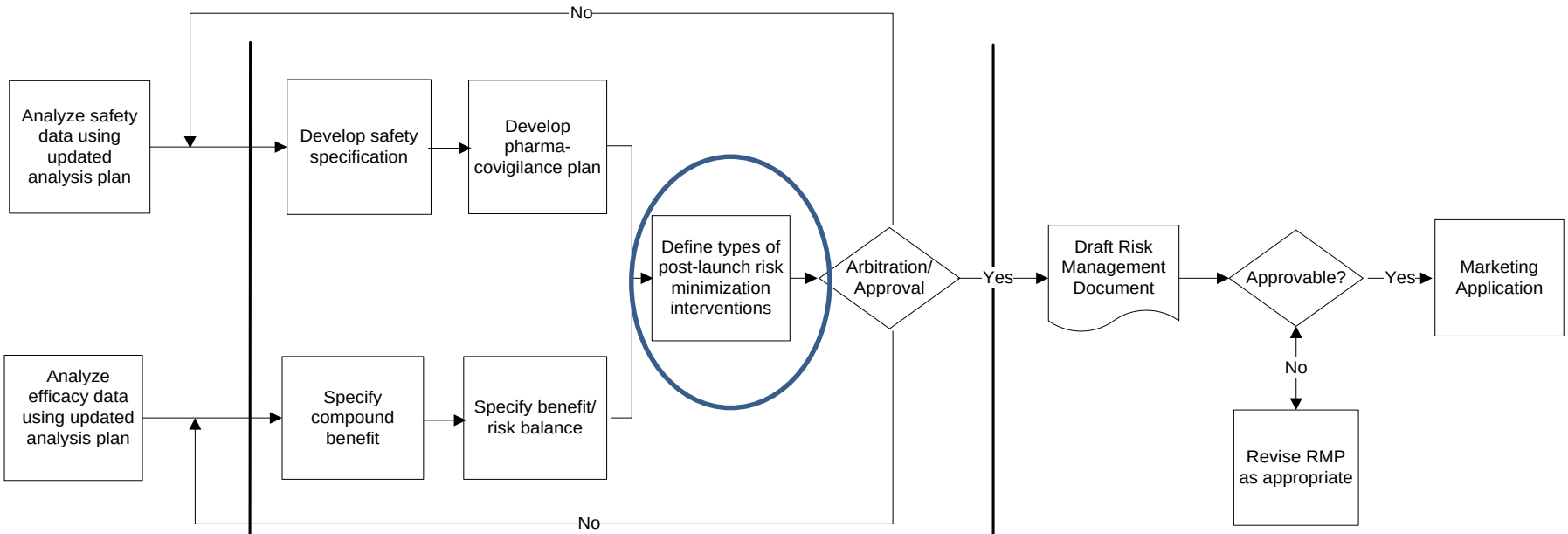
Authoring guide

Defines functions responsible for each section:

Part I	Product(s) overview
Part II	Safety specification
Module SI	Epidemiology of the indication(s) and target population(s)
Module SII	Non-clinical part of the safety specification
Module SIII	Clinical trial exposure
Module SIV	Populations not studied in clinical trials
Module SV	Post-authorisation experience
Module SVI	Additional EU requirements for the safety specification
Module SVII	Identified and potential risks
Module SVIII	Summary of the safety concerns
Part III	Pharmacovigilance plan (including post-authorisation safety studies)
Part IV	Plans for post-authorisation efficacy studies
Part V	Risk minimisation measures (including evaluation of the effectiveness of risk minimisation activities)
Part VI	Summary of the risk management plan
Part VII	Annexes

Preparation of RMP

Example



GPS responsible for safety data	GPS responsible for quantitative risk benefit analyses (when methodology available)	GPS, ABT(s) and PT collaborate, GPS assures public health perspective	Individual functions develop detailed interventions	GSIC owns template and manages RMP document
PT and ABT Medical responsible for efficacy data	PT and ABT Medical assess qualitative benefit/risk value; Marketing provides market value	GPLC advises on RMP		GPS VP, PT or Affiliate Medical Director sign off on final RMP(s). EU QP sign off on EMEA RMP.
Statistical support needed for both safety and efficacy analyses				

When to submit a RMP

- For all new marketing applications RMP describing the RMS for the medicinal product concerned, together with summary
- At any time during a product‘s life-cycle, i.e., during pre- and post-licensure phases
- Significant change in existing marketing authorization:
  - New dosage form
  - New route of administration
  - New manufacturing process of a biotechnologically-derived product
  - Pediatric indication
  - Other significant change in indication (e.g., new target population, a.o.)
- At request of Regulatory Authority when a concern about a risk affecting the Benefit / Risk balance
- At the time of renewal (if the product has an RMP)

Updates to the RMP

- If an RMP has previously been submitted, any following submissions must be in the form of an update
- Each RMPs must have distinct version number / date
- Clean and track-change RMP versions to be submitted
- Cover letter, detailing the changes since the last submitted version
- Submission of RMPs in general aligned with PSUR submissions
- If no changes since previous RMP submission MAH may submit a letter explaining that there is no change and not submit an RMP
- If requirement for providing routine RMP updates is not specified as part of MA routine RMPs to be provided:
  - annually until the first renewal of the MA
  - every three years thereafter

Ensure if National Authority accepts RMPs based on GVP with country-specific information in the cover letter

Preparation of RMP: Consistency with (e)CTD

RMP Module	eCTD
Part I Product(s) overview	Module 2.3 Quality overall summary Module 3 Quality
Module SI Epidemiology of the indication(s) and target population(s)	Module 2.5 Clinical overview
Module SII Non-clinical part of the safety specification	Module 2.4 Non-clinical overview Module 2.6 Non-clinical written and tabulated summaries Module 4 Non-clinical study reports
Module SIII Clinical trial exposure	Module 2.7 Clinical summary Module 5 Clinical Study reports
Module SIV Populations not studied in clinical trials	Module 2.5 Clinical overview
Module SV Post-authorisation experience	Module 2.5 Clinical overview
Module SVI "Additional EU requirements for the safety specification"	Data not presented elsewhere in eCTD
Module SVII Identified and potential risks	Module 2.5 Clinical overview (including benefit-risk conclusion) Module 2.7 Clinical summary (SPC)
Module SVIII Summary of the safety concerns	Module 2.5 Clinical overview Module 2.7 Clinical summary
Part III Pharmacovigilance plan (including post-authorisation safety studies)	Module 2.5 Clinical overview Module 2.7 Clinical summary
Part IV Plans for post-authorisation efficacy studies	Module 2.5 Clinical overview Module 2.7 Clinical summary
Part V Risk minimisation measures (including evaluation of the effectiveness of risk minimisation activities)	Module 2.5 Clinical overview Module 2.7 Clinical summary

Preparation of RMP: Consistency with PSUR

RMP section	PSUR section
Part II, module SV – "Post-authorisation experience", section "Regulatory and marketing authorisation holder action for safety reason"	Section 3 – "Actions taken in the reporting interval for safety reasons"
Part II, module SV – "Post-authorisation experience", section "Non-study post-authorisation exposure"	Sub-section 5.2 – "Cumulative and interval patient exposure from marketing experience"
Part II, Module SVII – "Identified and potential risks"	Sub-section 16.4 – "Characterisation of risks"
Part II, module SVIII – "Summary of the safety concerns" (as included in the version of the RMP which was current at the beginning of the PSUR reporting interval)	Sub-section 16.1 – "Summary of safety concerns"
Part V – "Risk minimisation measures", section "Evaluation of the effectiveness of risk minimisation activities"	Sub-section 16.5 – "Effectiveness of risk minimisation (if applicable)"

RMP versus PSUR

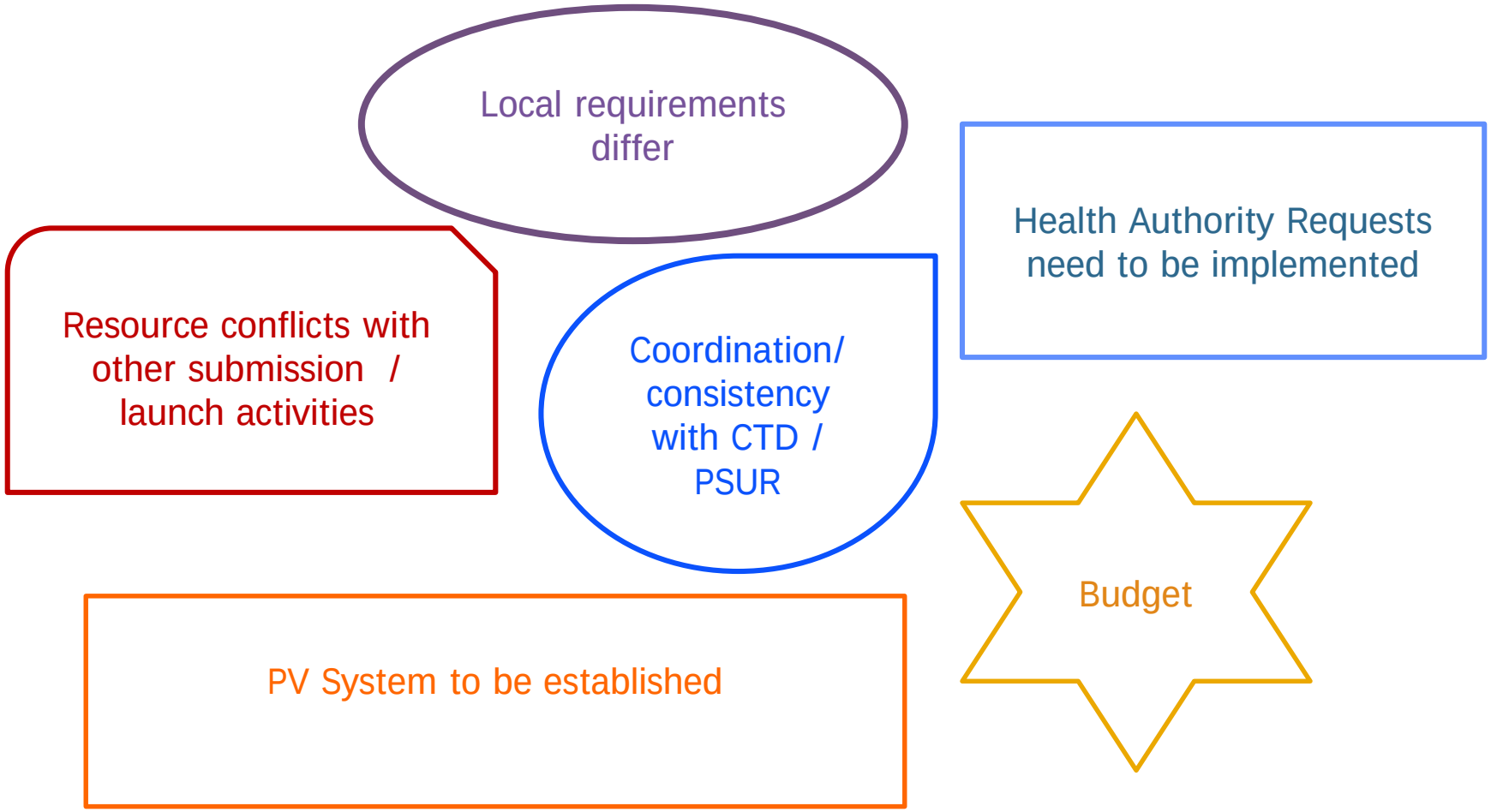
The two primary post-authorization PV documents

RMP	PSUR / PBRER
Main focus: **Pre- and postauthorisation risk-benefit management and planning**	Main focus: **Integrated post-authorisation risk-benefit assessment**
Risk minimisation plan	Ensuring benefit-risk balance remains favourable
PASS / PAES: data collection	Signal detection and evaluation
Risk minimisation measures	Establishing and documenting the „core safety profile“
Ensuring effectiveness of measures	Ensuring up-to-date product information

Tools to be used differently, depending upon where the product is in its life-cycle.

Challenges and complexities

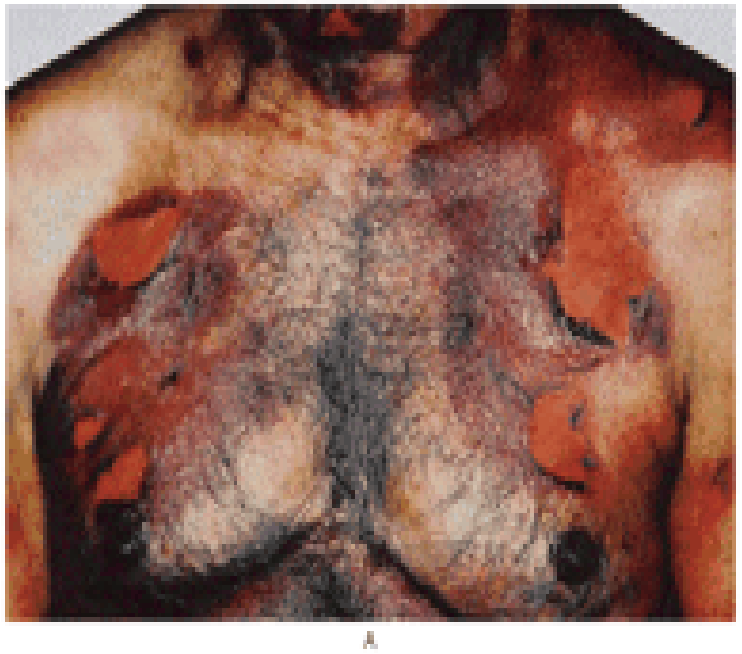
...include but are not limited to:



Important risks

An important risk?

Clearly an important risk!



Most discrepancies in understanding important risks are related to disability, life-threatening conditions or medical significance – as these assessments require medical judgement

Important identified / potential risks /1

Identified / potential risks:

- negative impact on the benefit – risk balance
- implications for public health
- depends on several factors:
  - impact on the individual patient
  - seriousness of the risk
  - frequency
  - preventability

In general:

any risk that is likely to be included in the contraindications / warnings and precaution section of the product information

Important identified / potential risks /2

Identified risk:

– Occurrence with an adequate evidence of an association with the vaccine.

Examples:

- Demonstrated in preclinical safety problems and observed in clinical trials
- AEFIs from clinical or epidemiological studies suggesting a causal relationship
- AEFIs suggested by a number of well-documented spontaneous reports with causality strongly supported by temporal relationship and biological plausibility

Potential risk:

– An untoward occurrence with suspicion of an association between the vaccine and the AEFI, the association, however, not confirmed.

Examples:

- Preclinical safety problems, not observed in clinical trials
- AEs from clinical or epidemiological studies, of which the risk parameters are suspicious for a safety problem
- AEFIs known from other vaccines with the same indication
- AEs to be expected based on the pharmacological action of the drug

Important identified risks for DTPw-HBV
Example

CIOMS Guide to Vaccine Safety Communication 2018

Example 3.2.3: The introduction of pentavalent vaccines in Kerala, India, supported by close interactions with the healthcare community and the media

A quadrivalent combined bacterial and viral vaccine protecting against diphtheria, tetanus, pertussis and hepatitis B, and was assessed by the European Medicines Agency (EMA) in collaboration with WHO, in order to facilitate its use in countries outside the European Union (EU). Based on the clinical trials, the following was classified as 'important identified risks': allergic reactions, high fever, convulsions, hypotonic-hyporesponsive episodes; and the following as 'important potential risks': apnoea in prematurely born children, fainting, brain disorder. In addition, the lack of safety and immunogenicity in children born prematurely was classified as 'missing information'. Given these safety specifications, no risk minimization measures other than the product information were considered necessary.[97] Information on the identified and potential risks, including warnings and precautions for use to minimize their occurrence and severity of impact, has been included in the package leaflets for carers and the healthcare professional information.[98, 99]

Risk Minimization Plan

When is a specific Risk Minimization Plan needed ?

- Not invariably but requires justification in the EU (approx. 18% of RMPs)
- Additional measures to mitigate known risks need to be :
    - Appropriate to the level of risk
    - Feasible in practice
    - Effectively communicated
    - Principles set at a global level but implementation according to local regulations/medical culture etc
    - Multi functional input and close coordination with affiliates important
- Current toolkit is limited
    - Need to be able to provide example (s) of proposed tools etc
    - Need to propose how effectiveness will be monitored; impact on spontaneous reporting unlikely to be acceptable

Risk Minimisation Measures (RMM)
Methods

- Information:
  - Product information for healthcare professionals (in the EU the SmPC)
  - Package leaflet (Patient Information Leaflet PIL)
  - Labelling on outer packaging
  - Training
  - Checklists
  - Educational material
  - Dear Healthcare professional communication (DHCP)
  - Pregnancy prevention program
- Prescribing restrictions (legal status):
  - In-patient use only
  - Specialised physicians only
  - Special administration
  - Controlled distribution systems

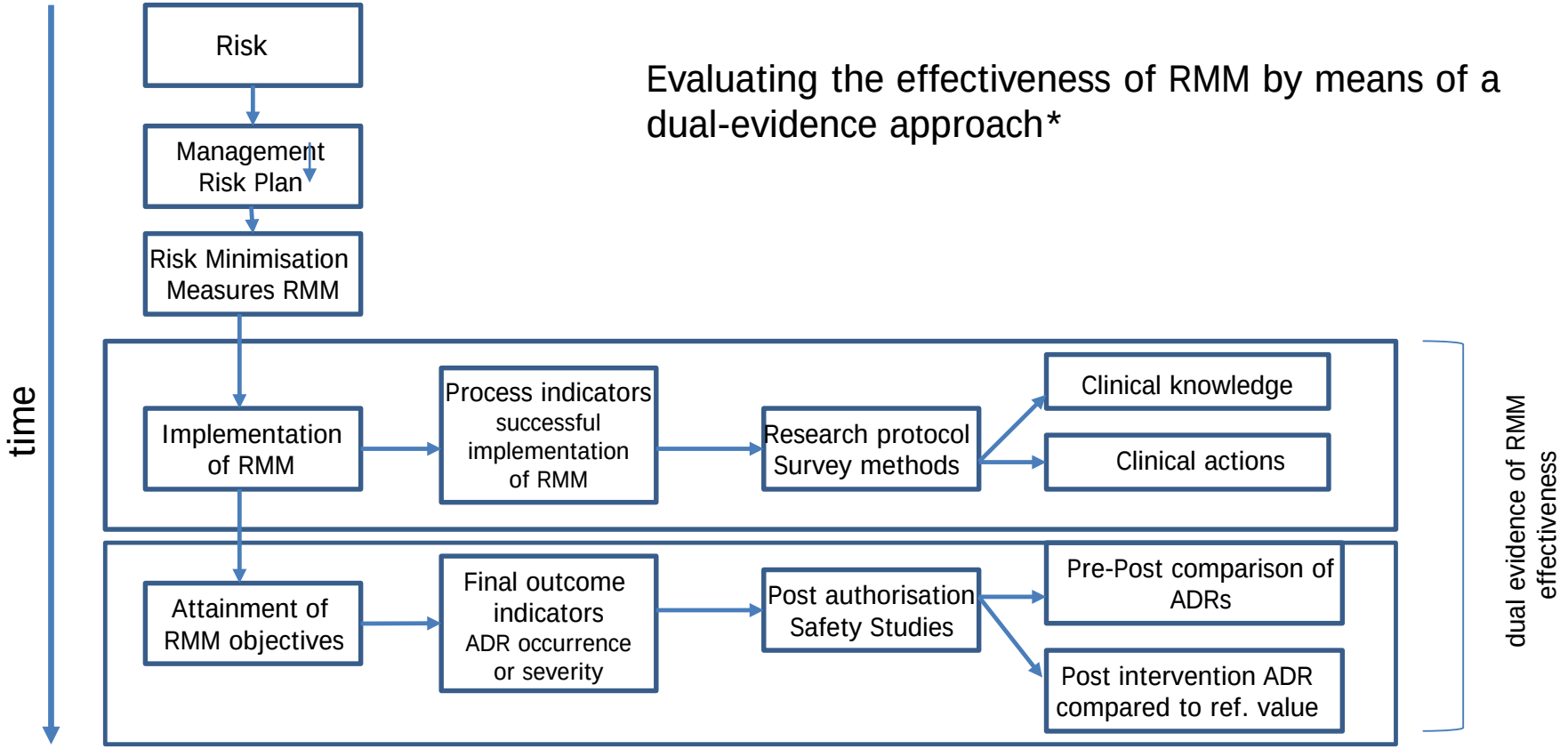
Rather drug specific:

Restrictions in quantity (e.g., doses / package unit)

Surveillance of the patients

- Registries
- Named patient use
- Restricted access programs
- ...

Risk Minimization Measures (RMM)
Evaluation of effectiveness



Evaluating the effectiveness of RMM by means of a dual-evidence approach*

*Pietro et al 2012

Safety Communication

HMA
Heads of Medicines Agencies

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

9 October 2017 2017
EMA/118465/2012 Rev 1*

Guideline on good pharmacovigilance practices (GVP)

Module XV – Safety communication (Rev 1)

Date for coming into effect of first version	24 January 2013
Draft Revision 1* finalised by the Agency in collaboration with Member States	17 November 2015
Draft Revision 1 agreed by the European Risk Management Facilitation Group (ERMS FG)	24 November 2015
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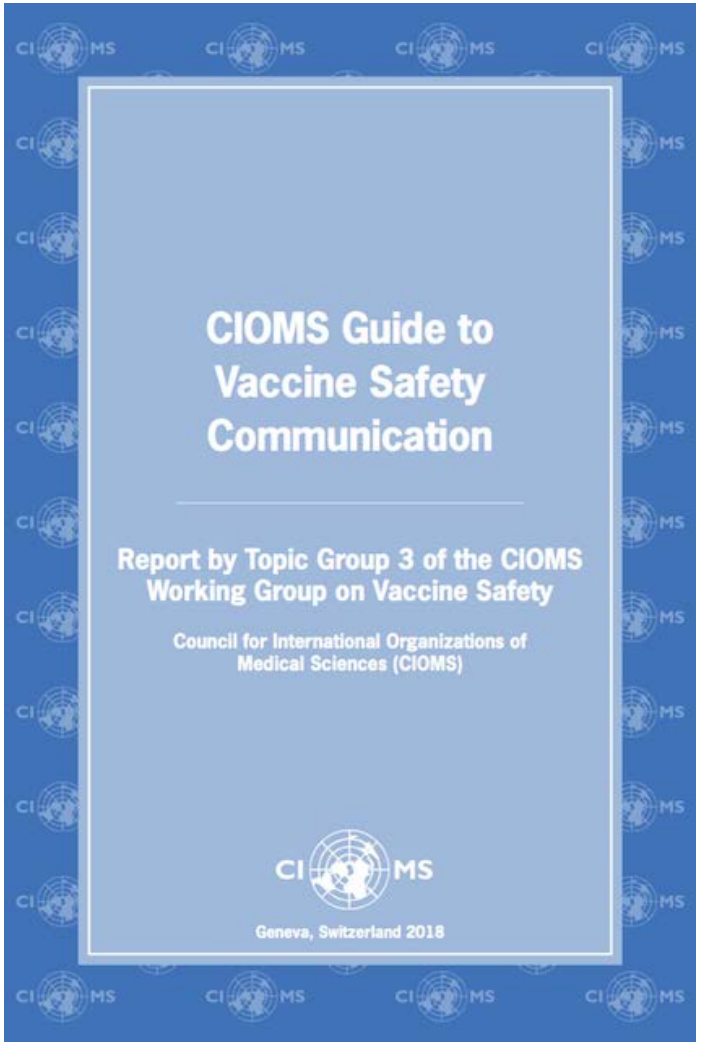
End of consultation (deadline for comments)	29 February 2016
Revised draft Revision 1 finalised by the Agency in collaboration with Member States	27 September 2017
Revised draft Revision 1 agreed by the EU Network Pharmacovigilance Oversight Group (EU-POG)	4 October 2017
Revised draft Revision 1 adopted by Executive Director as final	9 October 2017
Date for coming into effect of Revision 1*	13 October 2017



GVP Module XV Safety communication
Principles

- Provide timely and evidence-based information on the safe use of vaccines
- Deliver relevant, clear, accurate and consistent messages for the right audience at the right time
- Tailor to the appropriate audience by using appropriate language, respecting the different levels of knowledge and maintaining accuracy and consistency of the information
- Consider safety information communication throughout the PV and RM process as part of risk assessment and risk minimization measures
- Adequate coordination and cooperation between the different parties (e.g., Authorities, public bodies, MAH etc.)
- Present the risk in context of the benefits
- Address the uncertainties related to the safety concern
- Include risk on non-treatment as compared to risk of treatment
- Evaluate the effectiveness of safety communication, if possible

Safety communication – Vaccines
GVP PI

- Vaccine specific safety communication must
  - include information on avoiding errors in vaccine handling, administration and reiterating precautions and warnings
  - describe the benefits of vaccines
  - explain the risks for individuals and the population of a decrease in vaccination coverage
  - consider that risk perception may differ between stakeholders, esp. in case of uncertainty of a causal association
  - contain relevant background rates and exposure data when quantifying safety concerns.
- Communication planning must include preparedness for frequent public communication needs (e.g., on excipients, residues, identified or potential risks, coincidental events, temporal versus causal association, etc.).
- Regulatory Authorities must
  - ensure appropriate communication with public and media
  - maintain a high level of transparency on how regulatory decisions were reached.

Risk communication

- Black box warning
- Direct Healthcare Professional Communication (DHPC) letter (“Dear Doctor Letter”)
- Change of product labeling
- Publications
- Training
- Seminars
- ….

HMA
Heads of Medicines Agencies

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

8 December 2015
EMA/61341/2015

Guideline on good pharmacovigilance practices (GVP)
Module XVI Addendum I – Educational materials

Draft finalised by the Agency in collaboration with Member States for submission to ERMS FG	24 March 2015
Draft agreed by the European Risk Management Strategy Facilitation Group (ERMS FG)	30 March 2015
Draft adopted by the Executive Director	18 April 2015
Released for public consultation	27 April 2015
End of consultation (deadline for comments)	30 June 2015
Revised draft finalised by the Agency in collaboration with Member States	17 November 2015
Revised draft agreed by ERMS FG	24 November 2015
Revised draft adopted by Executive Director as final	8 December 2015
Date for coming into effect	16 December 2015

CIOMS
Vaccine Safety Communication Plan VacSCP
Template

1. Situation and Monitoring
   - Vaccine Safety
   - Epidemiology
   - Public
   - Monitoring of the public KAP, concerns, rumors and information needs
2. Communication objectives
3. Strategic design of the communication intervention
   - Target audiences
   - Change model
   - Key messages
   - Communication tools and dissemination mechanisms in a mixed media approach
   - Interactions with journalists and community advocated / activists
   - Timetable
   - Transparency provisions
4. Monitoring and evaluation

Risk Management Plans
Industry Experience

- Increasing trend to request EU specific RMP vs global document
    - e.g., wish to see specific reference to SPC sections vs generic statements relating to the CCSI
- Strong emphasis on paediatric use
    - May require a paediatric RMP
- Requests for :
    - studies in individual countries based on theoretical concerns
    - country specific PV activities / local RMPs where an EU RMP has been agreed
    - country specific utilization studies
    - Variable interpretation of what constitutes an important risk.....

Risk Management