EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

GVP Risk Management Systems

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An agency of the European Union

Main RMS items in PhV legislation

- RMP will be required for all new applications
- RMP should be proportionate to risks
- Key role of PRAC in relation to RMP
- PASS may be condition of MA
- PAES may be condition of MA
- Summary of the RMP to be made public
- Enhanced requirement to monitor the effectiveness of risk minimisation
- New definition of a RMP

Principles

IM very high level

Detail in GVP

Aligned with ICH E2E

Keep what has worked, change the less good

Risk Management Plan – purpose

- Identify or characterise the safety profile of the medicinal product(s) concerned;
- Indicate how to characterise further the safety profile of the medicinal product;
- document measures to prevent or minimise the risks associated with the product including an assessment of the effectiveness of those interventions;
- document post-authorisation obligations that have been imposed as a condition of the marketing authorisation

Dependent upon IM

Risk Management Plan - purpose

- Describe what is known and not known about the safety profile of the concerned medicinal product(s)

•Indicate the level of certainty that efficacy shown in clinical trial populations will be seen in everyday medical practice and document the need for studies on efficacy in the post-authorisation phase.

- Plan how the effectiveness of risk minimisation measures will be assessed

The "Pick and Mix" RMP

Changes to the basic structure

Current RMP structure

Part I

Safety Specification

Pharmacovigilance Plan } **ICH E2E**

Part II

Evaluation of the need for risk minimisation activities,

if a need for additional activities

- **Risk minimisation plan**

RMP structure in IM

Part I	Product(s) Overview
Part II	Safety Specification
Part III	Pharmacovigilance Plan
Part IV	Plans for post-authorisation efficacy studies
Part V	Risk Minimisation Measures
Part VI	Summary of the RMP
Part VII	Annexes

Modules in safety specification

Module S1: 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 S.S.

Module SVII: Identified and potential risks

Module SVIII: Summary of the Safety Concerns

Dependent upon IM

New yet original?

S1: Epidemiology of the indication(s) and target population(s).

SII: Non-clinical part of the Safety Specification

SIII: Clinical trial exposure

SIV: Populations not studied in clinical trials

SV: Post authorisation experience

SVI: Additional EU requirements for the S.S.

SVII: Identified and potential risks

SVIII: Summary of the Safety Concerns

- Non clinical
- Limitations of the human safety database
- Populations not studied in the pre-authorisation phase
- Post marketing experience
- Adverse events/adverse reactions
- Identified and potential interactions with other medicinal products, food and other substances
- Epidemiology of the indications and important adverse events
- Pharmacological class effects
- Additional EU requirements
- Summary – ongoing safety concerns

SIV: Patients not studied in clinical trials

Paediatric population

- Age categories (1st introduced in update to Vol 9a)

Elderly population

- More emphasis on upper end of spectrum
- Effect of multiple impairments and multiple medications
- ADRs of special concern in elderly – dizziness, CNS

Immunocompromised including organ transplant patients

Specific genetic markers

SVI: Additional EU requirements

Potential for harm from overdose

Potential for transmission of infectious agents

Potential for misuse for illegal purposes

Potential for medication errors

Specific paediatric issues

- Issues identified in Paediatric Investigation Plans
- Potential for paediatric off label use

Projected post-authorisation use

Potential for off label use

Part IV: Plans for post-authorisation efficacy studies

Studies on long term safety +/- efficacy requested in past

Efficacy in legislation for paediatric medicines and ATMP

Ability to require post-authorisation efficacy studies in new PhV legislation

Logical extension of pharmacovigilance planning

Post authorisation development plan will improve resource utilisation

Part IV: Plans for post-authorisation efficacy studies

Will be used for developing public summary

Summarise efficacy and basis for this – ie studies and endpoints (1 page)

Short review of where fits into therapeutic armamentarium

Robustness of endpoints and need for further study

Applicability of efficacy studies to all patients in target population

Consideration of studies to ascertain which patients will benefit most

Summary of the RMP: Preliminary ideas

One size unlikely to fit all!

Still have “summary table” in the EPAR

Public Summary of the RMP aimed at lay people

Planned consultation in May with stakeholders – including patients and HCPs

Summary of the RMP: Preliminary ideas

Based on parts of S1, SVIII, Part IV, Part V

Provide context of risks

- Overview of disease epidemiology, expected benefits and where medicine fits into therapeutic armamentarium

Summary of safety concerns in lay language

Planned post-authorisation efficacy and pharmacovigilance studies

Summary of safety concerns and risk minimisation activities

Public health issues

Need to be able to have studies covering multiple drugs

Problem of patient registries

- Comparators
- Generics

Problem of multiple forms of educational material for same active substance.

Public Health: *very draft proposals*

Joint studies: Article 10a….the Agency shall *encourage*…….

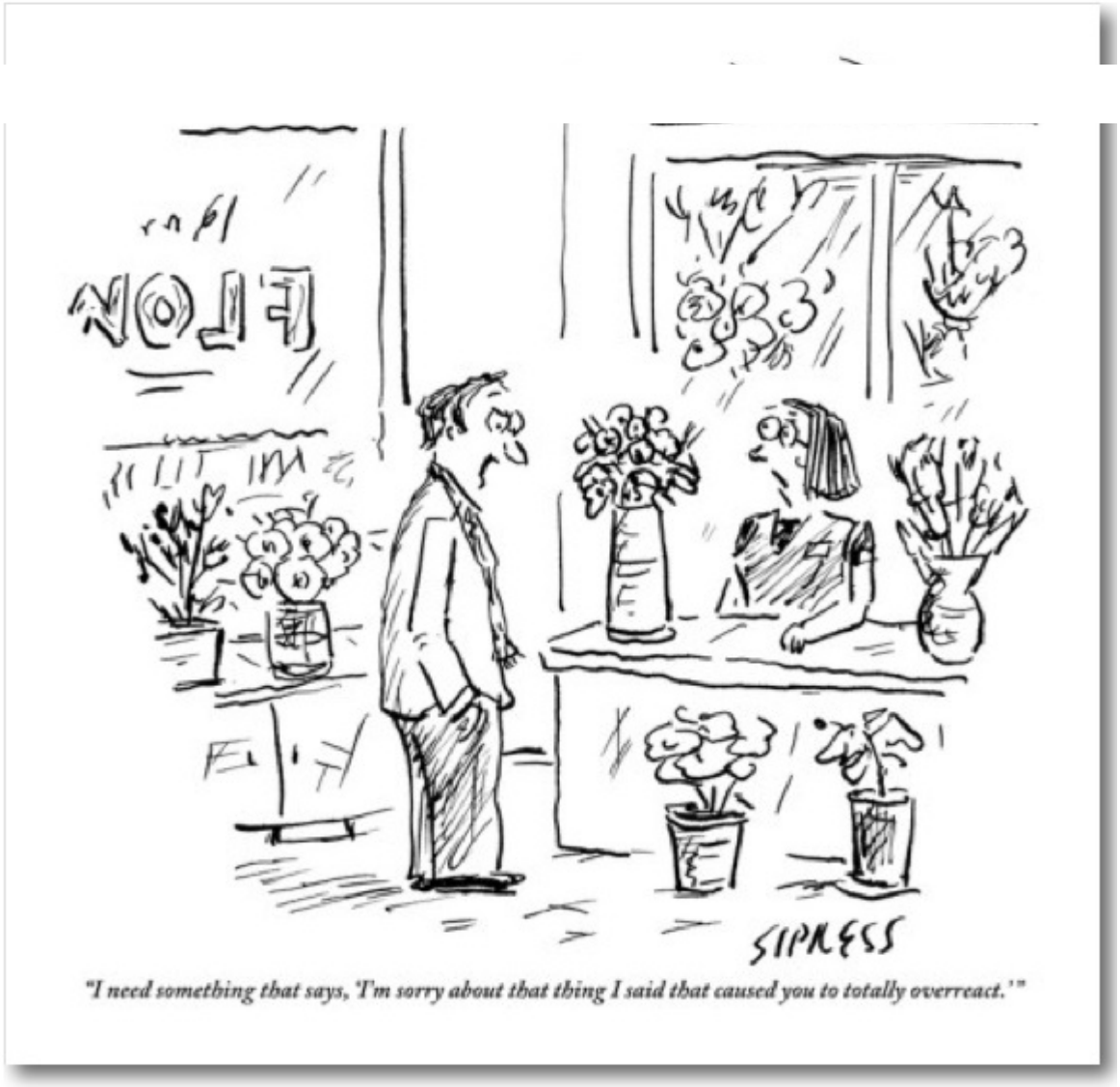
- Agency will propose a core protocol if failure by MAHs to agree joint study

One registry regardless of which brand of drug prescribed

Educational material should look the same for reference products and generics

Conclusions

- RMP guidance overhauled to reflect new legislation and experience since 2005
- Change to modular structure to make it easier to satisfy different regulatory needs
- Important new areas include:
  - a new Public Summary which will be written for lay people
  - A new part IV on plans for post-authorisation efficacy studies



"I need something that says, 'I'm sorry about that thing I said that caused you to totally overreact.'"