efpia
European Federation of Pharmaceutical Industries and Associations

AESGP

EGA

Building on Perspectives of 3 years of operation of the EU Pharmacovigilance Legislation; **Opportunities for the Future**

EuropaBio®
The European Association for Bioindustries

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On behalf of the

Industry Associations

Vaccines Europe
An industry for healthy lives

ACRO
ASSOCIATION OF CLINICAL RESEARCH ORGANIZATIONS

EUCROF
European CRO Federation

ebe
european biopharmaceutical enterprises

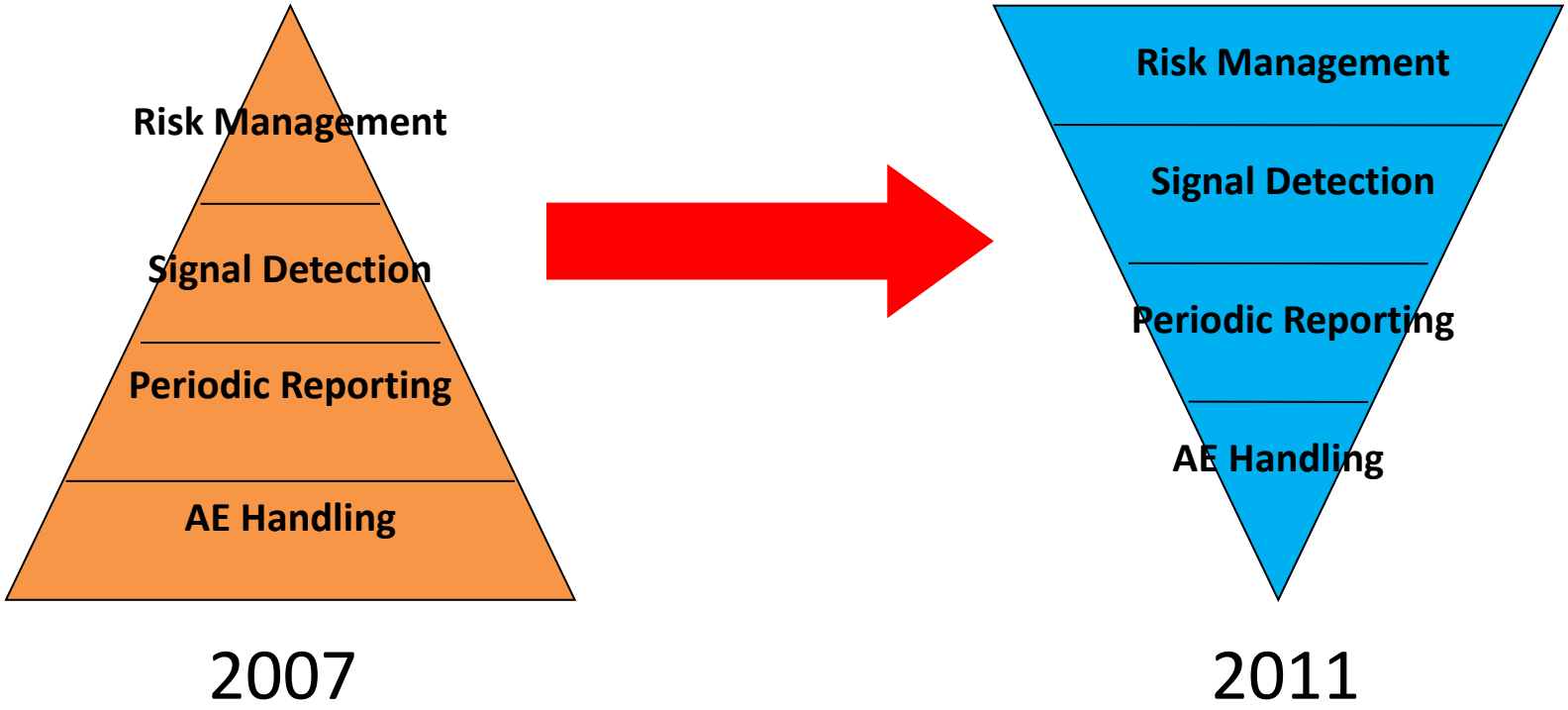
EUCOPE
European Confederation of Pharmaceutical Entrepreneurs AISBL

In this presentation

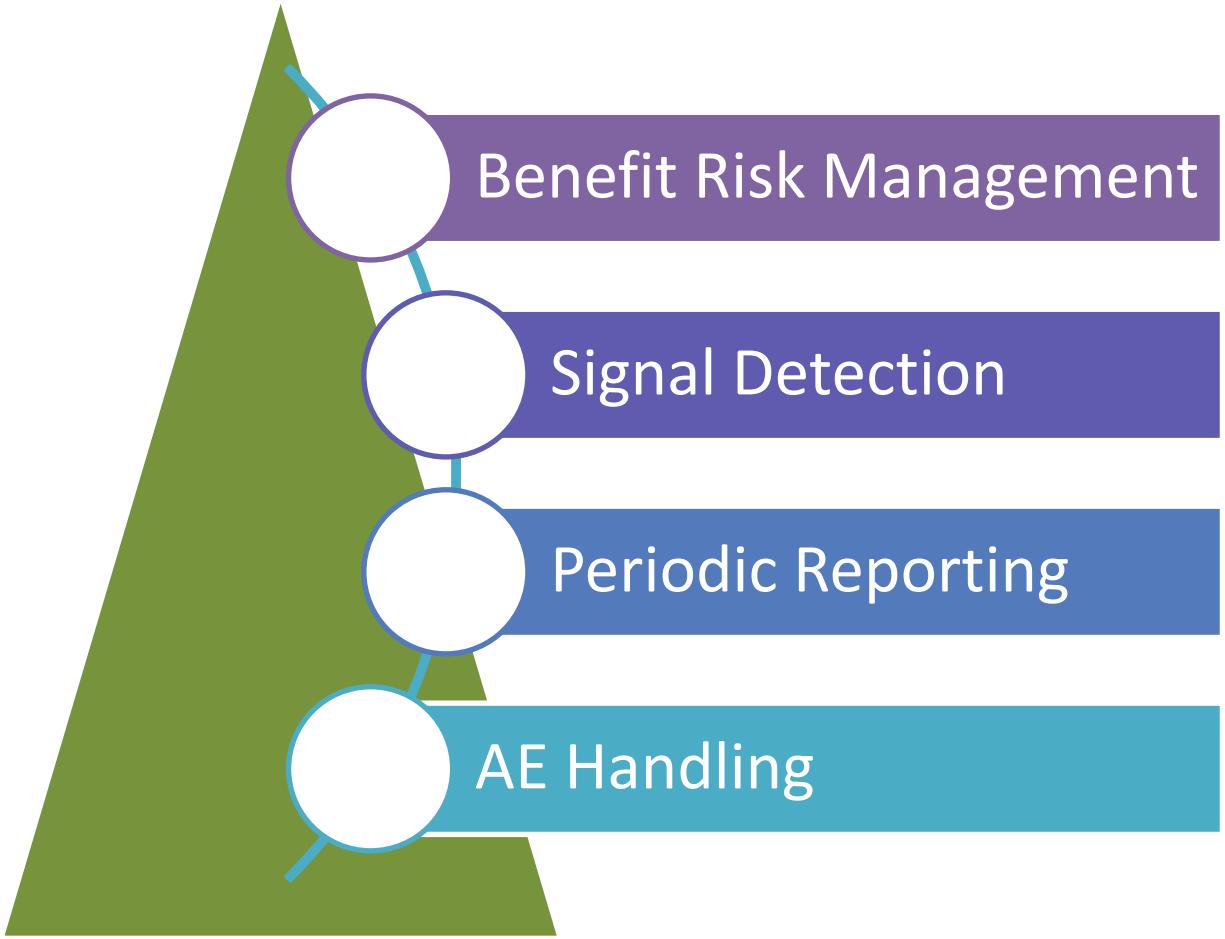
- **Reflect the key outcomes of the legislation** – achievements and improvement possibilities
- **Demonstrate the "real feeling"** through examples
- **Present the view on "success factors"**
- **Present the view on the most important areas where to apply these factors:**
  - Individual Safety Case Reports
  - Periodic Safety Update Review (PSUR)/Periodic Benefit-Risk Evaluation Review (PBRER)
  - Risk Management Plan (RMP)
  - Benefit-Risk Framework
- **Summary**
- **Proposals for the future**

In Collaboration

Pharmacovigilance in the Future
A Complete Shift in Emphasis ?



Fast forward to 2015 post new legislation Implementation



Aims of the New EU Pharmacovigilance Legislation – Where have we got to ?

- Collection of better data on medicines and their safety; ✓
- Rapid and robust assessment of issues related to the safety of medicines; ✓
- Effective regulatory action to deliver safe and effective use of medicines; ✓
- Empowerment of patients through reporting and participation; ✓
- Increased levels of transparency and better communication. ✓

The legislation includes significant implications for marketing-authorisation applicants, holders and service providers. It aims to:

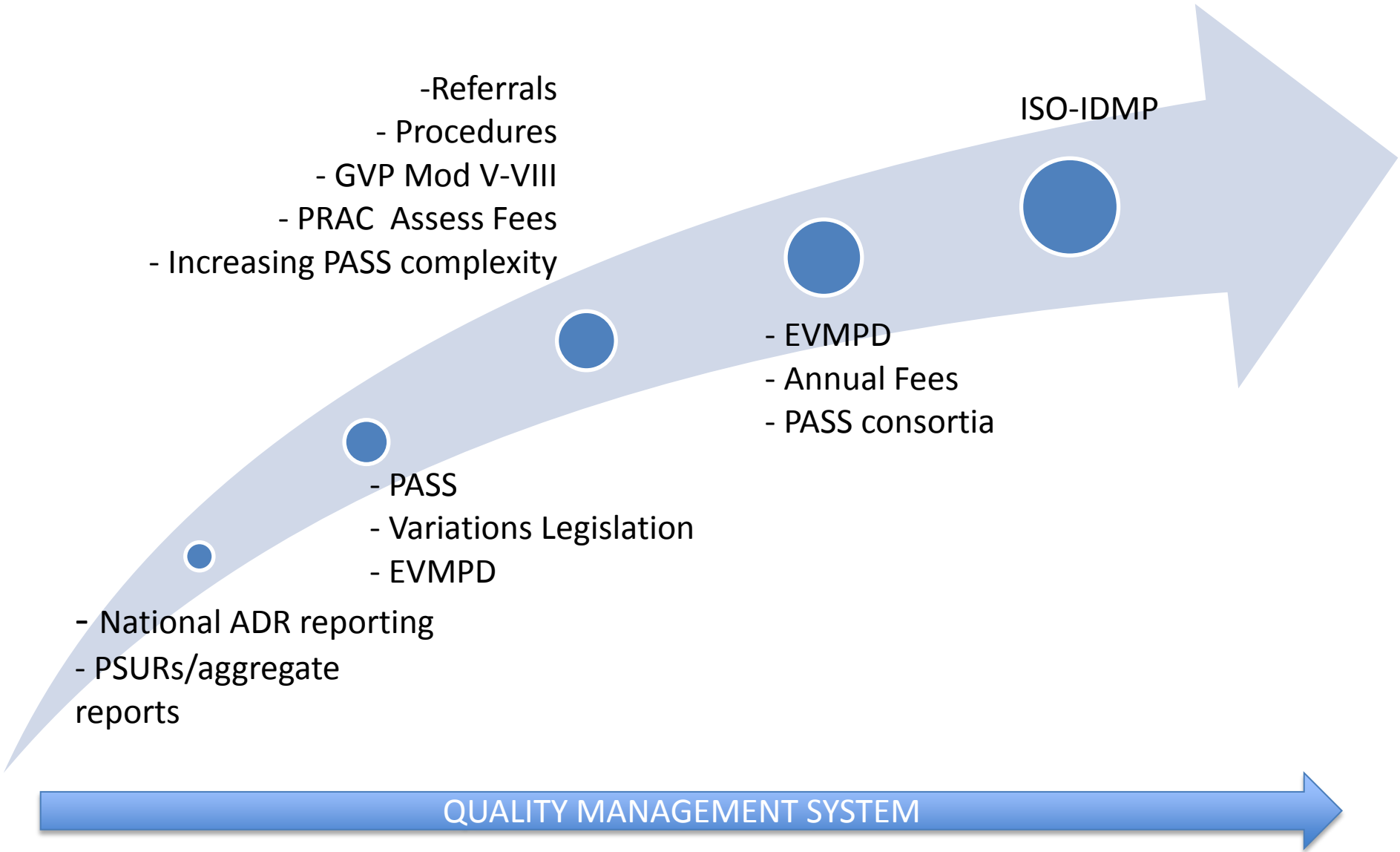
- Make their roles and responsibilities clear; ✓
- Minimise duplication of effort; ✓✗
- Free up resources by rationalising and simplifying reporting on safety issues; ✗
- Establish a clear legal framework for post-authorisation monitoring. ✓

Burden Varies on Different Players

- **Large Multi-National Companies**
  - Change management across company globally (many of whom outside EU)
  - Implementation across multiple departments (many outside pharmacovigilance)
  - Liaison with multiple licensing partners & CROs
  - Multiple products (complexity of scale)

- **SME's**
  - Implementation overwhelming (e.g only 1 person responsible for pharmacovigilance)
  - Challenges for grouping and in adapting to consortium
  - Fees for PSUR, PASS and Referrals have a higher impact on medicines which have a low turnover and those that may only be approved at a local market.

Increasing Complexity with Time and into the Future



Example on Complexity- Post Authorisation Safety Studies (PASS)

Requirements detailed in:

- PV Legislation
- Guidance GVP Modules
- Variations Regulation
- Post-authorisation Q&As
- RMP and other templates
- PV Fees Legislation

Against backdrop of increased costs:

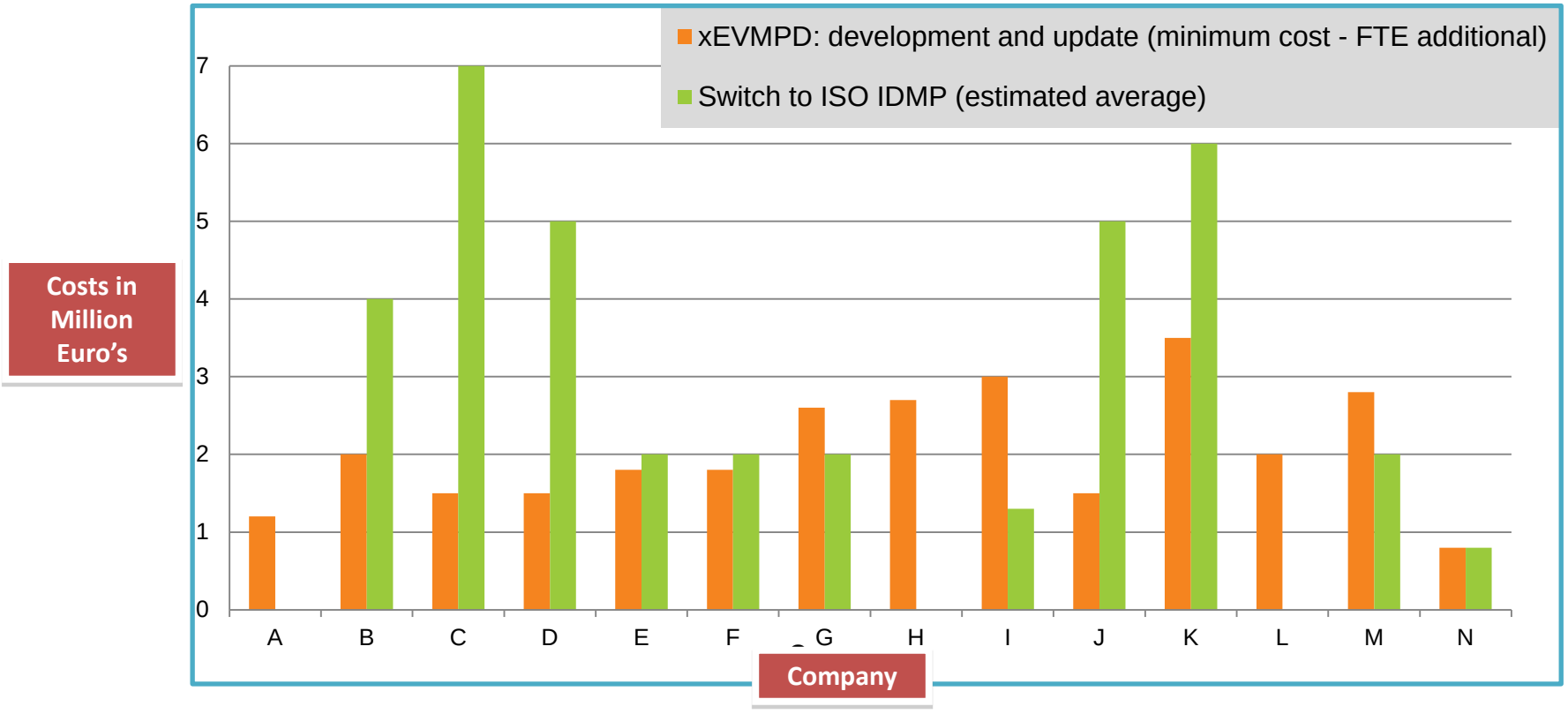
- IDMP
- EudraVigilance
- CT Regulation (depending on implementation)
- Falsified Medicines Directive (depending on implementation)

- Confusing legislation has led to inconsistent implementation
- Inconsistent processes for centralised and national / MRP products
- Inconsistent application of the requirements by regulators

The system has become too complex and provides a detraction from scientific focus and a potential source for additional compliance risk for involved operators

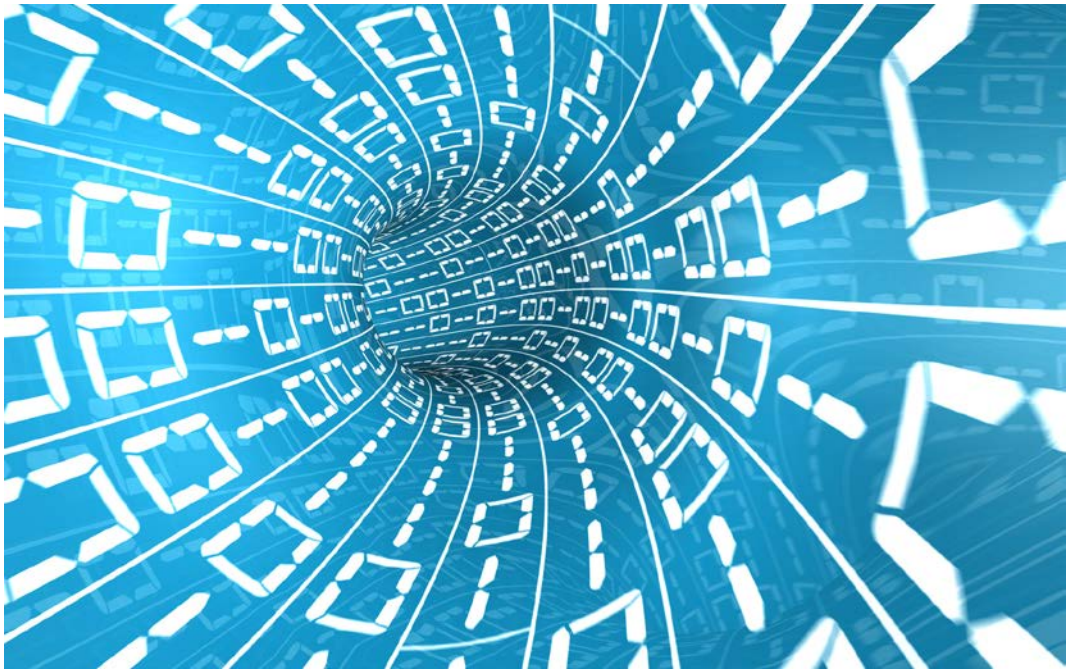
Example on Costs – Predicted cost (€m): xEVMPD development & ISO IDMP switch

- A sample of 14 EFPIA companies spent a total of at least **€28M** on their **xEVMPD** implementation
- A sample of 11 EFPIA companies are expecting to spend a total of at least **€38M** on their **ISO IDMP** switch



Example on Technical burden: PATIENT CENTRICITY

As IT simplification is not reached yet, mainly due to the **technical complexity**, both industry and authorities are still struggling with technical issues taking resources from concentrating on patient safety



Key Factors for future

Simplify

Risk –based approach

"The ability to simplify means to eliminate the unnecessary so that the necessary may speak." - Hans Hoffman

Example on “Risk-based approach”: FUTURE OF INDIVIDUAL CASE SAFETY REPORTS

- Large volumes of poor quality data from Interactive Digital Media, Market Research Programs and Patient Support Programs (PSP) do not lead to better signal detection or signal evaluation

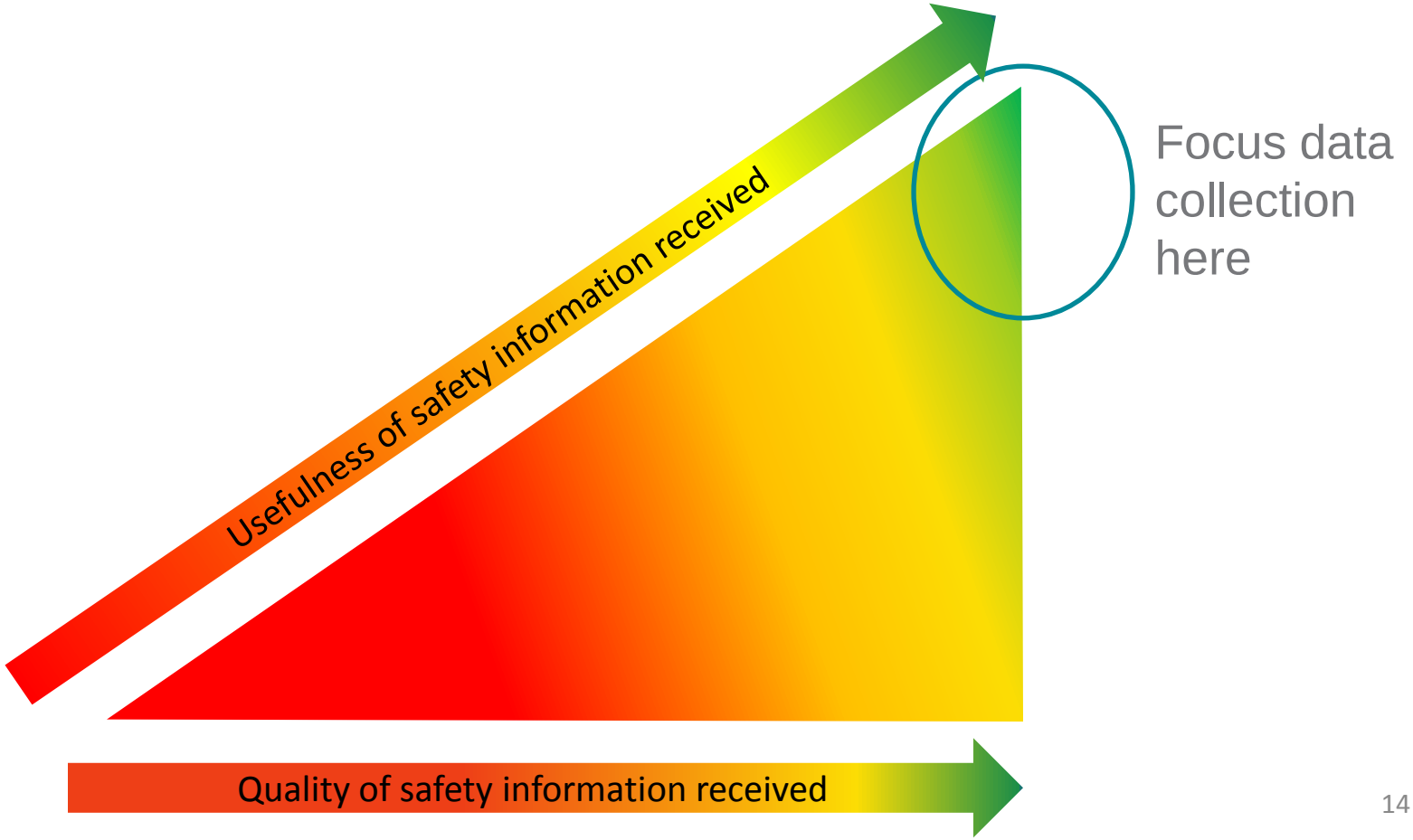
- Focussing on reports of suspected ADRs is more likely to generate useful data and will enable better use of resources at MAHs and NCAs and less burden on healthcare providers and patients

- Using technology to identify signals and trends in external data sources, e.g. social media

- Industry and regulators need to work together to find pragmatic solutions that allow focus on the most important data sources and issues

INDIVIDUAL CASE SAFETY REPORTS Target

- Risk-proportionate data collection and focus



Future of PSURs/PBRERs

- Refocus on ICH E2C(R2) Standards and Principles
- Consistent with legislation and GVP Module VII
  - Maintains the spirit of harmonisation for a document submitted internationally
- Alignment of expectations
- Focus on informative summaries vs extensive raw data and multiple reviews
- Discourage “ gold plating”/tailoring to individual needs
- Consider publishing the ICH E2C(R2) Q&A

Future of RMPs

- Refocus on ICH E2E and ICH E2C(R2) Principles:
  - Risks in RMPs should reflect that ADRs are not the same as risks/important risks
  - Important risks should be focused on clinically important ADRs which have medically significant **outcomes**
    - Be reasonably expected to have substantial and clinically demonstrable impact on patients/public health

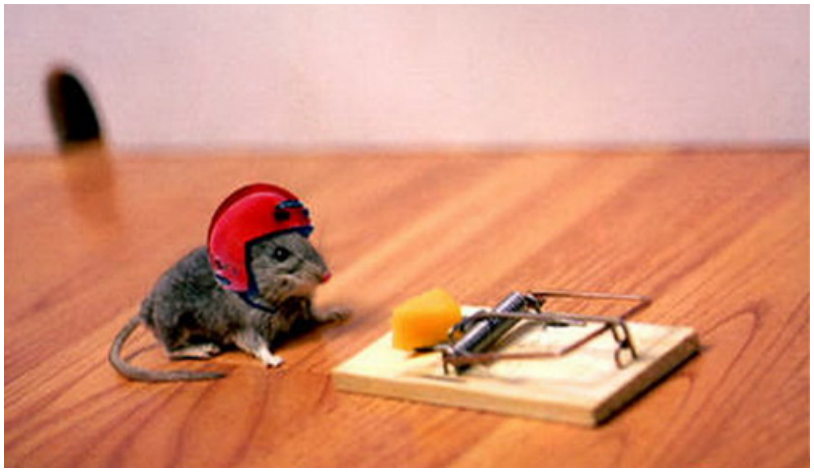
*"A risk may not be important if it is infrequent, non-serious, reversible, and readily managed with no significant impact on the individual patient or public health."**

*"Even a common ADR may not constitute an important risk if it is not linked to clinically significant adverse sequelae."**

* ICH E2C(R2) IWG Q&A 2014

Benefit-Risk Holistic View

Registry strategy



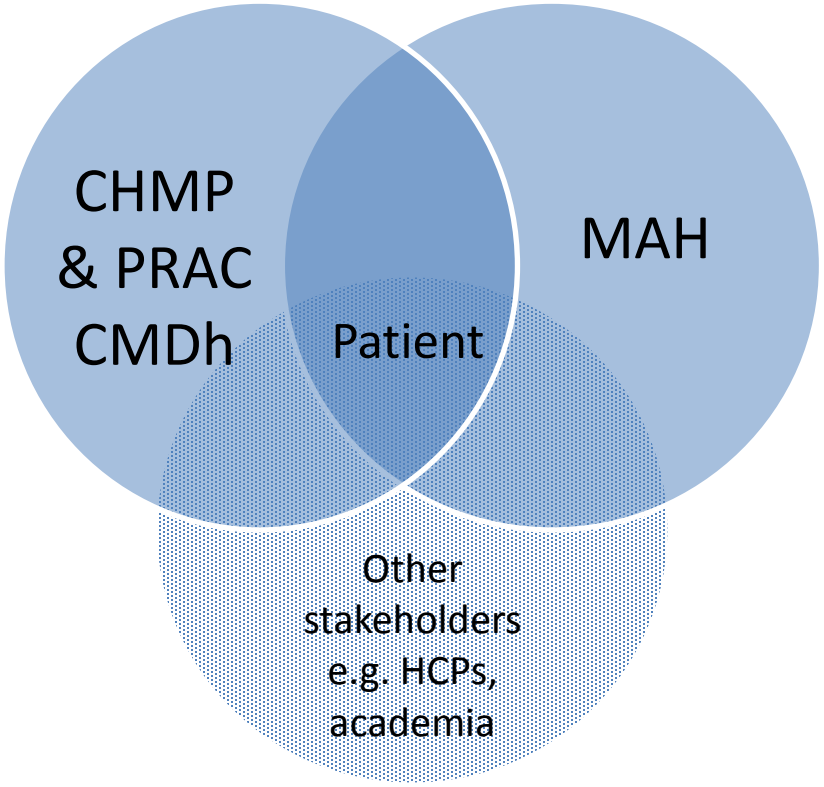
B/R methodolgy

Assessment of data-generated pre-approval in clearly defined patient population (CHMP led with PRAC input)

RMP-PASS-PAES

Assessment of data-generated post-approval in real-world context (PRAC led with CHMP input)

Benefit-Risk Assessment Framework



A framework with the patient at its centre, which supports an informed benefit-risk decision in the context of the relevant disease

In Summary

- **Burden being felt by all and has resulted in some change in Regulator's focus:**
  - PRAC is moving its focus from "Compliance" to "Optimisation"
  - EMA is focusing on simplification activities

- **PV Platform meetings providing a much appreciated opportunity** for MAHs to raise concerns and seek alignment (CROs to be included?)

- **Working on practical solutions together very useful**

e.g. literature monitoring pilot/ PSUR repository

Industry Proposals for the future

- **Focus on what is most likely to impact patient safety and public health**
  - For data collection concentrate on sources most likely to generate quality information
  - In Periodic Safety Update Reports and Risk Management Plans focus on important risks

- **Convergence to allow compliance with legislation and guidance on a global basis**
  - Consistent with international consensus

- **Proportionate and pragmatic approach for MAHs, CRO's, Inspectors, HCPs and patients**
  - Based a on common understanding e.g for PSPs and PASS