



ProductLife
GROUP

Consulting and Outsourcing for Life Sciences

Risk management and the future of Pharmaco Vigilance

Product Life – Erick GAUSSENS CSO

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.COM**

Agenda

- Short ProductLife Presentation
- Some of the key issues of Volume 9A
- The concept of proactive safety
- The challenges for PV



- Experts in Information Systems (IS) for Life Science R&D
 - ✓ e submission of all nature (eCTD, eIND, PIM, SPL, ASMF, PIP, E2B) and all dematerialization initiatives (Electronic Lab Note Book, eCRF,...)
 - ✓ electronic document management, product life cycle management, portfolio tracking, proactive safety management, non-clinical systems harmonization
 - ✓ training
- Strategic consulting on business process
 - ✓ process change management (governance, SOPs, training...): Regulatory activities optimization, proactive safety governance and operations, development project optimization, ICH Q9/Q10
 - ✓ IS governance/strategies and associated risk evaluations
 - ✓ integration of BPO in R&D/Manufacturing strategies
- Outsourcing (as such or as a continuum with above points)
 - ✓ Esubmission
 - ✓ regulatory activities
 - ✓ data base management (regulatory, raw materials, contracts, bibliography....)
 - ✓ all back office works: scanning, OCR, indexing, biblio searches, archiving supportOffice templates

E-Research and Development

Risk Management

- proactive safety
- industrial risks
- frauds and counterfeits

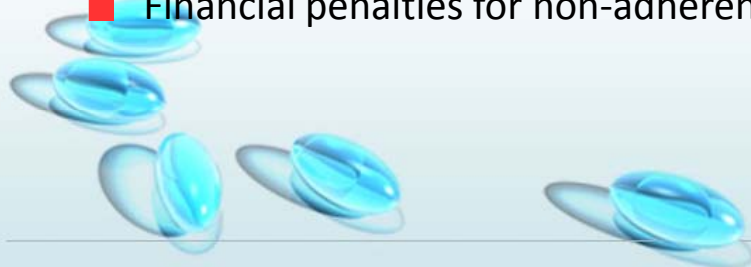


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- **Some of the key issues of Volume 9A**
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- Eudralex Vol. 9a:
 - Eudralex are Rules governing Medicinal products in the EU.
 - Eudralex Vol 9a deals with Pharmacovilance concerning medicinal products for human use
- Target of the new legislation:
 - Adequate protection of public health, without delaying the timely access to medicines for patients
- Components:
 - Responsibilities of Qualified Person
 - Submission of Risk Management Plans in MAAs
 - Benefice/ Risk balance assessment throughout the life cycle of medicines
 - Mandatory electronic reporting by NCAs and MAHs
 - Revision of PSUR periodicity
 - Specific PV requirements for Centrally Authorised Products from target patient groups; expand CAPs:
 - Biotech products, orphan products, NCEs for AIDS, cancer, neurodegenerative disorder, diabetes ...
 - Financial penalties for non-adherence to legal obligations

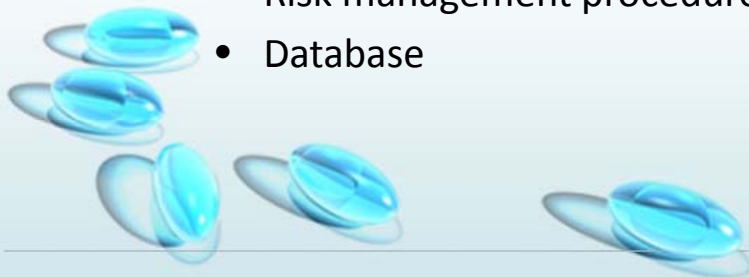


- Each MAH should:
 - appoint one QP responsible for overall PV for all medicinal products for which the company holds MAs in the EEA
 - adequately support the QPPV and ensure that there are appropriate process, resources, communication mechanisms and access to all sources of relevant information relating to the evaluation of the Risk Benefice Balance.
 - Be able to provide detailed description of PV system :

- QP
- Organization, links with other organizations, SOPs
- Database
- Documentation, Quality system, Training

For instance, among procedures to establish, those concerning:

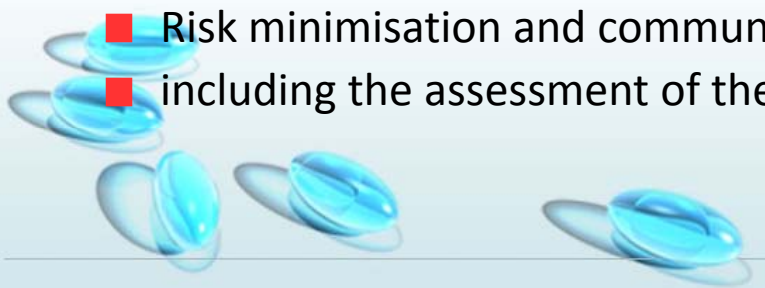
- Continuous safety monitoring, signal generation and review, benefit risk assessment, notifying changes to CAs
- Risk management procedures for RMPs
- Database



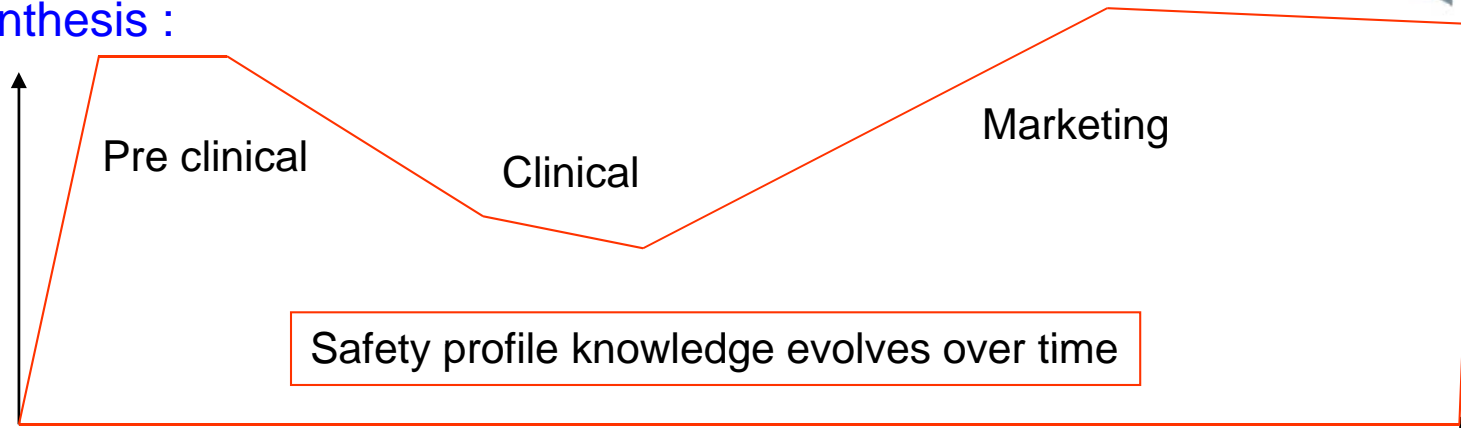
- The QPPV is responsible for:
 - preparing reports for HA:
 - ICSR (Individual Case Safety reports)
 - all serious cases (expected or unexpected) even those occurred outside EEA
 - To be submitted electronically (EUDRAVIGILANCE)
 - MAH has to enter retrospective data (from 1995, jan 1st) for non EEA cases via EUDRAVIGILANCE (Authorities enter EEA cases)
 - PSUR (Periodic Safety Update Reports) :
 - change of periodicity of reporting
 - NB : Head of Medicines proposes synchronization of PSURs:
 - » Harmonization of product birthdates and synchronization of PSUR of products authorized through national or Mutual Recognition Procedure
 - Company sponsored post authorization safety study
 - Reporting of ADR
 - Interim and final study report
 - providing input into Risk Management Plan



- A Risk Management System for an individual medicinal product or a series of medicinal products can be presented to Competent Authorities in the form of an EU Risk Management Plan (EU-RMP) .
- EU-RMP describes (a template exists):
 - Safety specification
 - Pharmacovigilance plan
 - Risk minimisation activities
 - Appendices : Study designs, Methods for risk minimisation
- EU-RMP is an output of an intensive drug monitoring system focusing on :
 - Risk detection
 - Risk assessment
 - Risk minimisation and communication interventions
 - including the assessment of the effectiveness of these interventions.



A first synthesis :



Compliance:

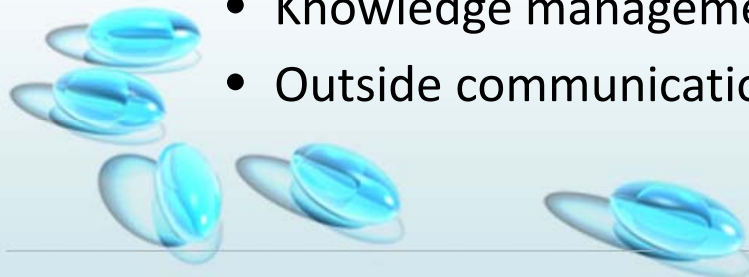
- E2B Electronic Reporting and EVDMS
- Clinical Safety
- Periodic Safety Reporting
- Affiliates
 - Inbound Receipt and Triage
 - Outbound Submission Tracking
 - Safety to Investigator Reporting

Commitment:

- Workflow and Metrics on safety reporting
- Bibliographical searches, data Mining and Quantitative/Qualitative Signal Detection
- Safety Profile Tracking
- Risk Mitigation / Minimization
- Risk Management Planning and Metrics

Some first statements

- The expectations derived from Volume 9A change the role of Safety within our organization and toward the external world
- They suppose a strong effort to analyze which commitments and which strategies we want to follow for each of our products: **a governance**
- They deeply affect our practices in terms of information management:
 - Referential
 - Knowledge management
 - Outside communication



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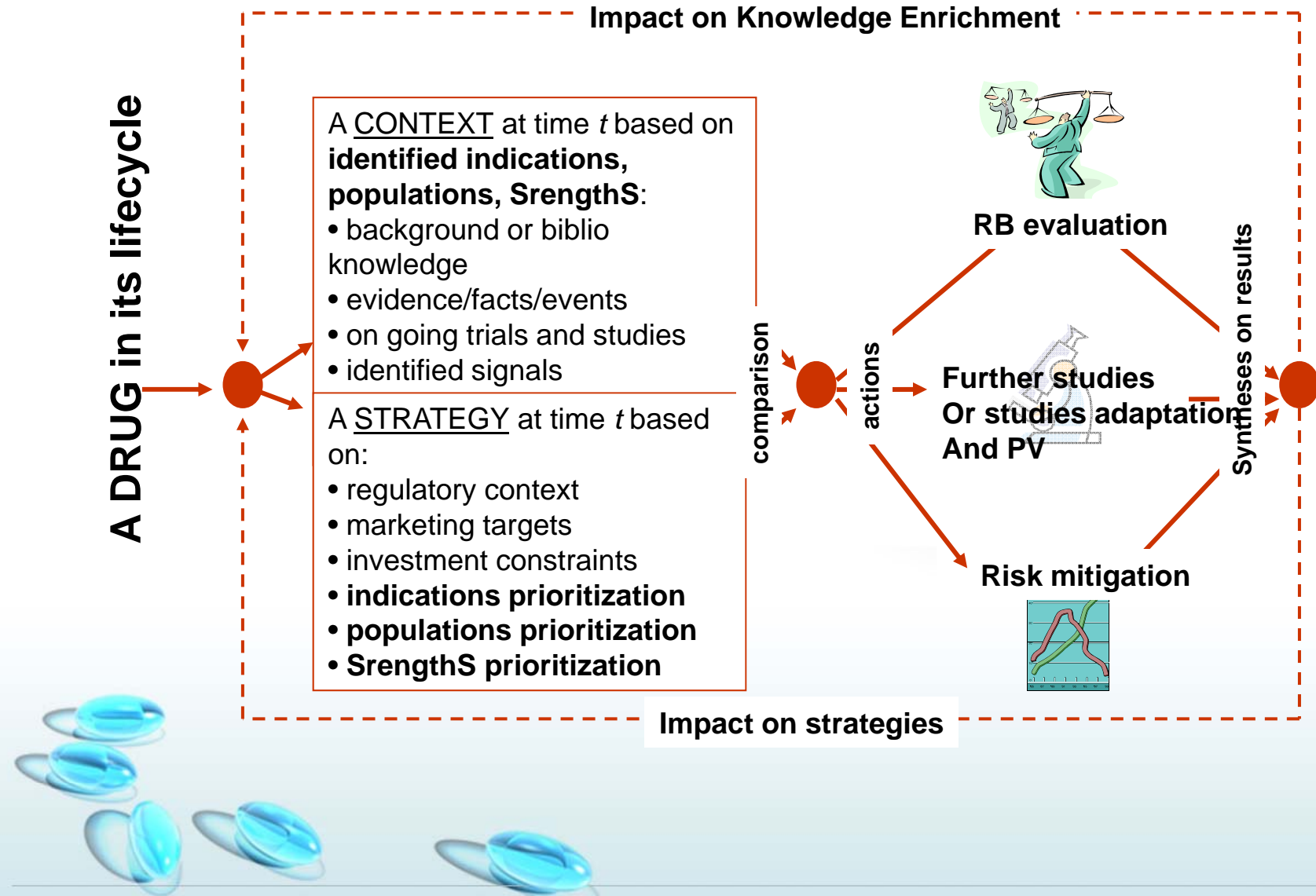


Pro Active Safety concepts

- To integrate safety not only as a constraint but as a driving force to market our products => Benefit Risk Balance
- To more efficiently manage compliancy by realizing that information management from all sources:
 - R&D
 - Regulatory
 - Supply chain and manufacturing
 - PV
 - Medical Information and links with Health Professional
 - ...

Have to be somehow accessible and coordinated





NB: Signals and related methods are Quantitative and/or Qualitative

- mechanism analysis in literature
- unexpected chemical behavior
- unexpected cell behavior
- unexpected symptoms on animals
- interim/final trials results
- AE during clinical trial
- AE on marketed product
- (ph-) epidemio studies protocols

- applicability
- repeatability
- contextual interpretation
- links with the drug/product
- case analysis
- + frequency, exposure
- (ph-) epidemio studies analysis

2) Signal/results understanding



- setting up experimental targets
- analytical studies defining protocols
- PK/PD analysis, new protocols
- PK/PD, stat methods, severity
- individual case analysis
- (ph-) epidemio studies concl

1) Signal/results capture

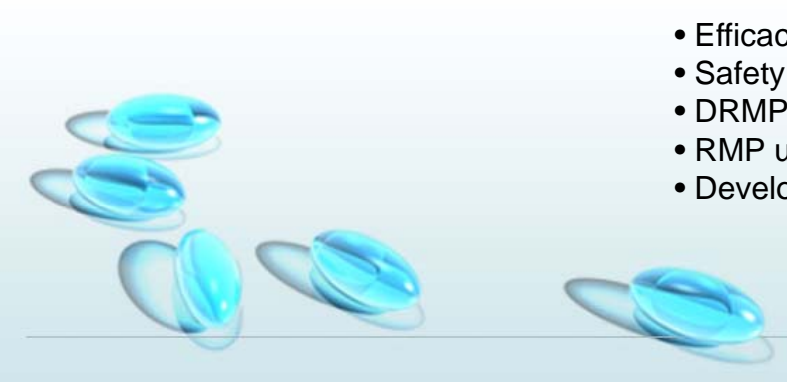
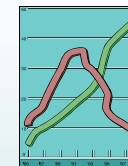
- Background knowledge
- Planned actions

3) Risk/evidence elicitation

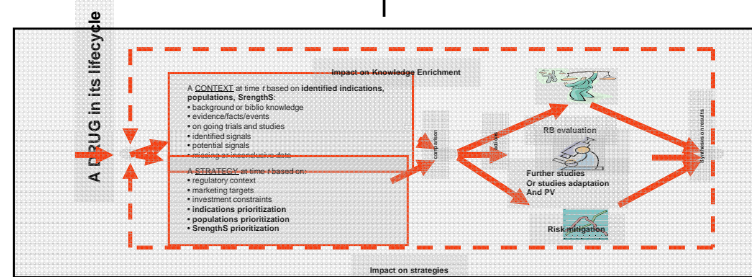
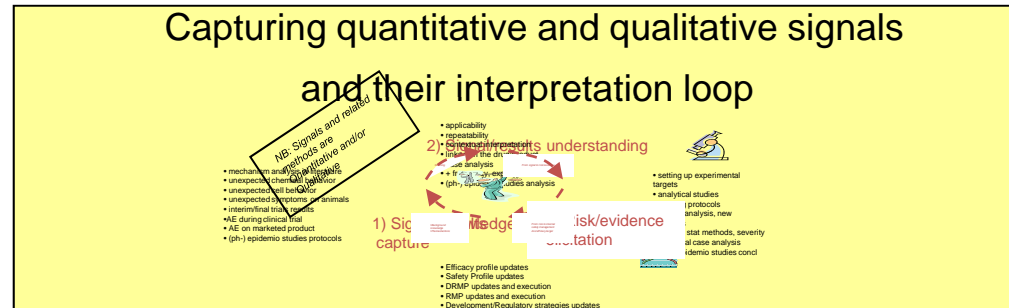
- From risk to internal safety management
- And efficacy target

4) Knowledge/Actions Management

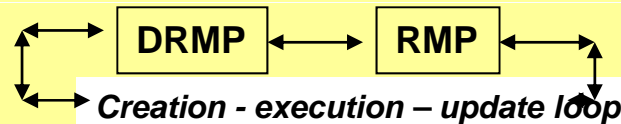
- Efficacy profile updates
- Safety Profile updates
- DRMP updates and execution
- RMP updates and execution
- Development/Regulatory strategies updates



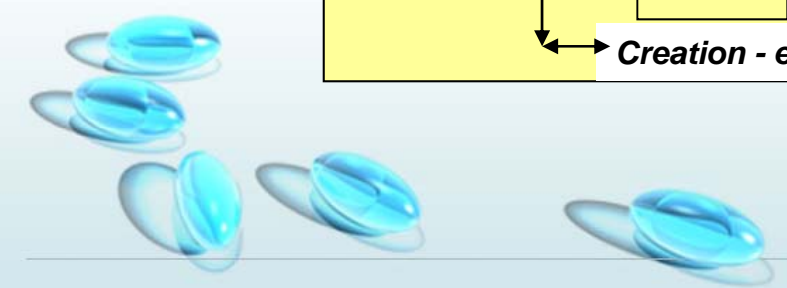
BR Knowledge Basis/portal



Formalizing internally the output of the pro active safety process
An evolving reference document



Decision Dashboard

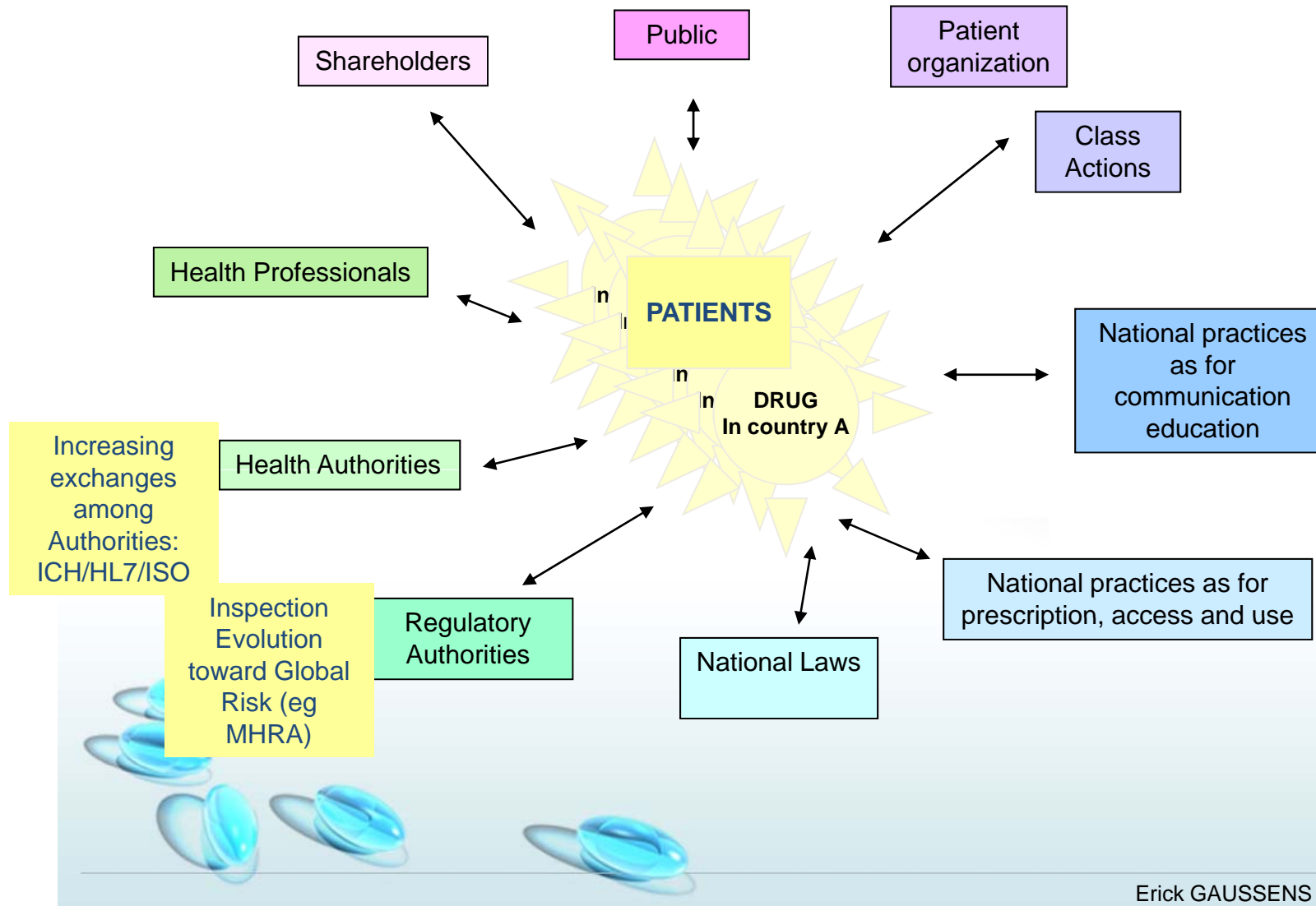


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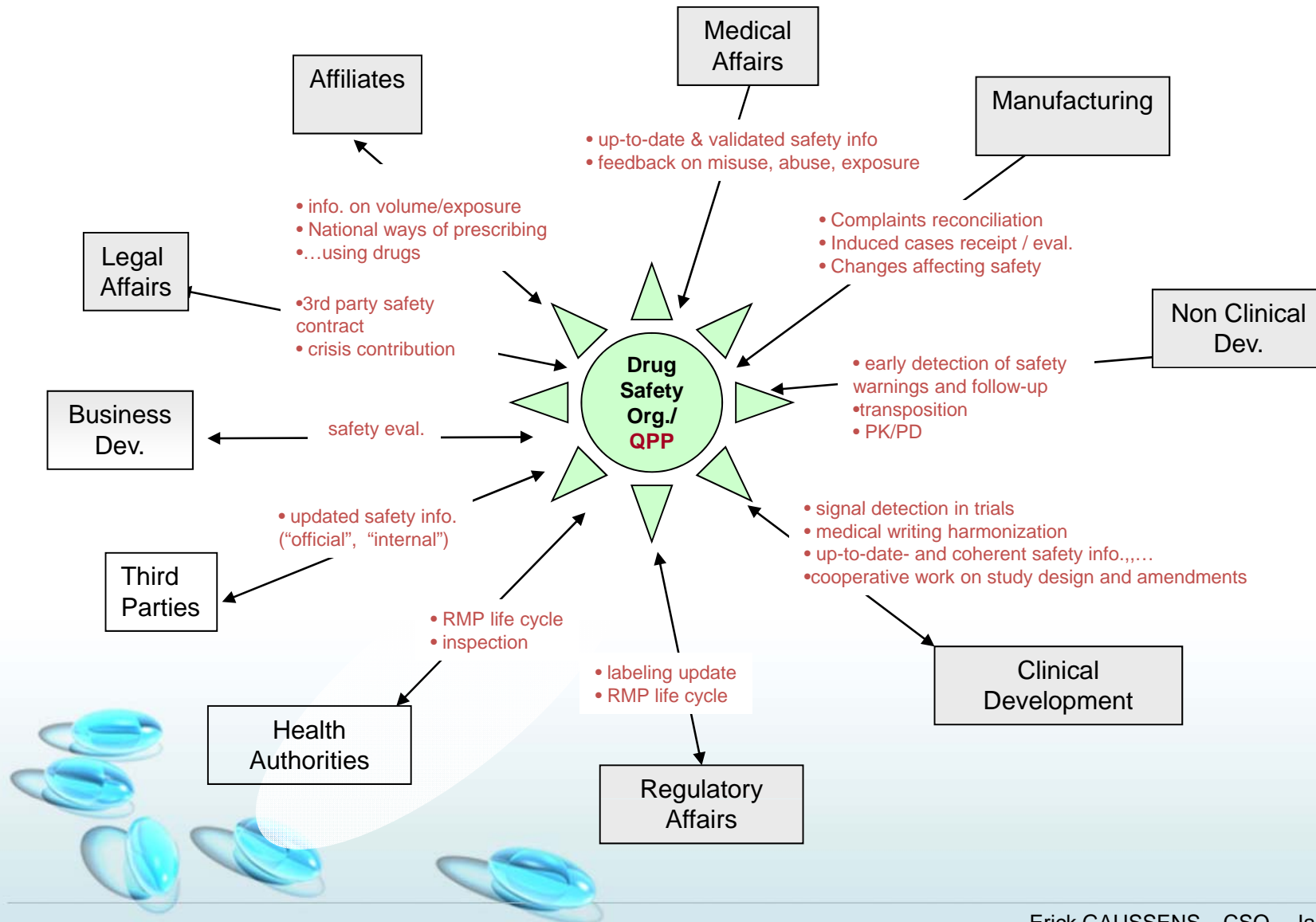
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An external complexity :



An internal complexity :



The PV Challenges : organization

- To work on world wide basis
- To work within an extended team framework
- To integrate a proactive safety global approach
- To get prepared to the “global Risk” inspection approach as claimed eg by MHRA
- while keeping the compliancy level to which the Company is committed or will commit after its own interpretation of the regulations and guidelines



The PV Challenges : Information Management

- To access to all information linked with drug A in country X at time T patient exposure:
 - Approved AAM and approved prescription information
 - “version” of the product available
 - Batch release
 -

- To access to all safety related information:
 - On going RMP, on going commitments for product A in country X at time T, PSUR/line listing history
 - Drug safety profile and B/R balance history
 - Company's strategy versus communication and marketing

