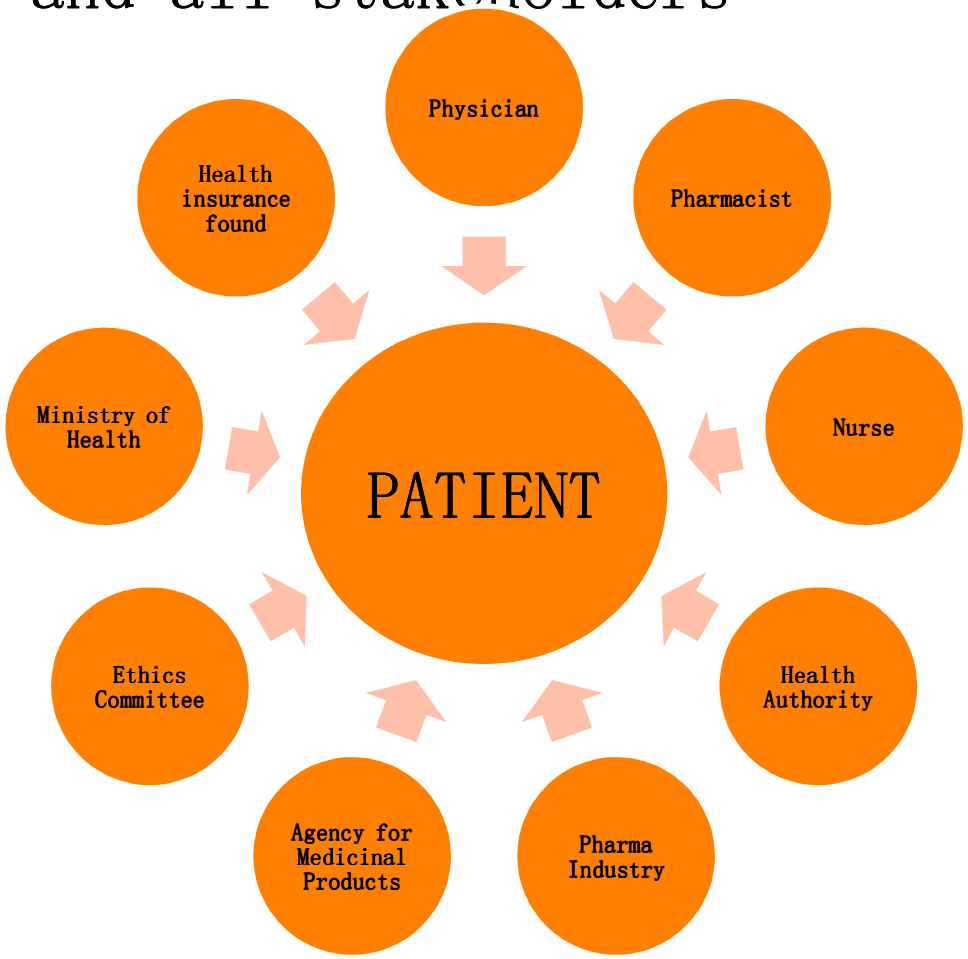
Industry pharmacovigilance practices

Symposium: ‘’ Current Regulatory Aspects in the Field of Medicinal Products and Medical Devices in Human and Veterinary Medicine’’, 14th & 15th November 2014, Vršac

Alma Nukić, MPharm
Roche Croatia

Innovative global pharmaceutical industry
…and all stakeholders…

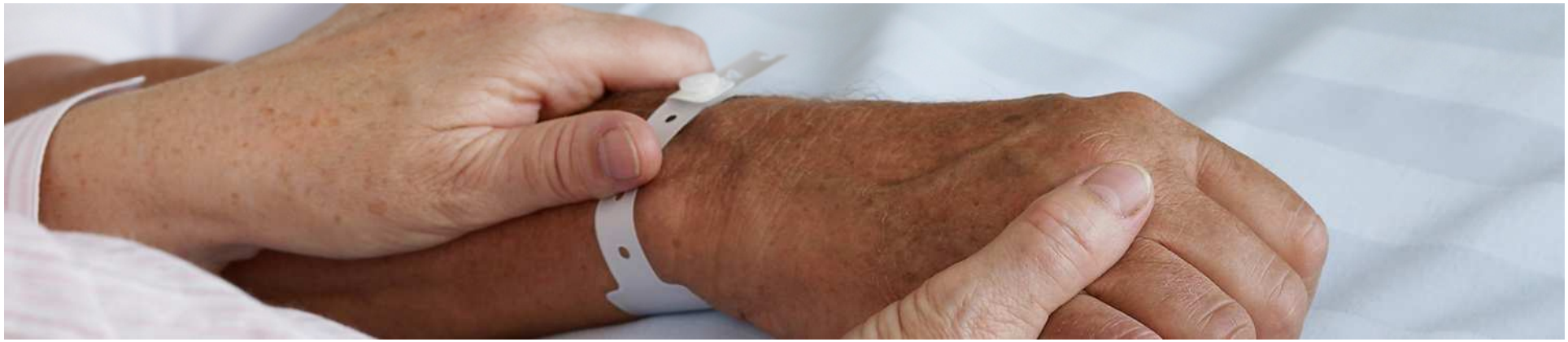


Our priority is to make sure that the therapeutic benefits of the medicine out
throughout the lifecycle of a medicine.

Innovative global pharmaceutical industry
…and all stakeholders…

Patient safety is of paramount importance to us.

We should ensure that use of (innovative) medicines is safe.



Focus on Pharmacovigilance

First of all, How do we work?

UNDER LEGAL FRAMEWORK: local, global (e.g. EU legislation)

Focus on Pharmacovigilance

CROSS FUNCTONAL: safety, regulatory, quality…

Focus on Pharmacovigilance

EMA webpages

‘’ The new pharmacovigilance legislation, which started to come into effect in July 2012, was the biggest change to the regulation of human medicines in the European Union (EU) since 1995. It had significant implications for applicants and holders of EU marketing authorisations.’’

Adoption of **new Directive and Regulation** by the European Parliament and Council of Ministers in December 2010, bringing about significant changes in the safety monitoring of medicines across the EU:

- Directive 2010/84/EU
- Regulation (EU) No 1235/2010
- Regulation (EU) No 1027/2012 (applicable since 5 June 2013)
- Directive 2012/26/EU (applicable since 28 October 2013)

Focus on Pharmacovigilance

EMA webpages…

~~Volume 9A~~

‘’ Practical measures to facilitate the performance of pharmacovigilance in accordance with the legislation are available in the **guideline on Good pharmacoVigilance Practices (GVP)**. GVP apply to marketing-authorisation holders, the European Medicines Agency and medicines regulatory authorities in EU Member States, and cover medicines authorised centrally via the Agency as well as medicines authorised at national level.’ ’

GVP modules I to XVI cover major pharmacovigilance processes.

The **chapters on product- or population-specific considerations** are currently under development. (public consultation is ongoing for P II Biological medicinal products)

Guidelines should be followed!

GVP Modules

I Pharmacovigilance systems and their quality systems

II Pharmacovigilance system master file

III Pharmacovigilance inspections

IV Pharmacovigilance audits

V Risk management systems

VI Management and reporting of adverse reactions to medicinal products

VII Periodic safety update report

VIII Post-authorisation safety studies

IX Signal management

X Additional monitoring

GVP Modules

XI Public participation in pharmacovigilance (public consultation 4Q 2014/1Q 2015)

XII Continuous pharmacovigilance, ongoing benefit-risk evaluation, regulatory action and planning of public communication (public consultation 4Q 2014)

XIII (Incident Management → Module XIII on incident management is no longer under development. All topics originally intended to be covered in this module are now to be included in module XII.)

XIV International cooperation (public consultation 1/2Q 2015)

XV Safety communication

XVI Risk-minimisation measures: selection of tools and effectiveness indicators

+ annexes

Pharmacovigilance processes

Nowadays we do not just report and processing adverse events/adverse drug reactions but **we are deeply involved in and do also:**

- Signal detection
- Risk Management Plan
- Safety Communication
- Study and Program Oversight
- Aggregate Reports
- PV Quality
- PV Agreements
- Labeling and PV Commitments

Signal detection

DATA SOURCES: data from the clinical and safety database, pre-clinical data, Phase 1 data in healthy volunteers or patients, spontaneous reports, internet or social media sites created or sponsored by the Company, Registries, Epidemiological databases, health care databases

Signal Detection Plan

RMP
Risk management activities

We want to have a safe treatment as much as possible… we need to create a Plan (Risk Management Plan)

Risk Minimization Activities are present in all industries not just pharma!

The aim of a risk minimization activity is to reduce the probability or severity of an adverse reaction.

- routine risk minimization (e.g., product labeling)
- additional risk minimization activities (e.g. patient communications/educational materials)

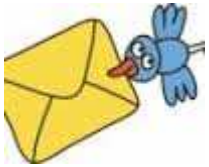
RMP
Educational Materials

- Approved by national Agencies

Have we distributed the right educational material to relevant HCPs and patients with valid outcome?

We need to monitor and measure effectiveness, the process (distribution) and outcome.

Safety Communication




- Report in a timely manner

- Providing timely, evidence-based information on the safe and effective use of medicines

- Dear Healthcare Professional Communication (DHPC)
- Dear Investigator Letter (DIL)
- To Whom it May Concern Letter (TWIMCL)
- Safety Queries
- Local/global crisis management

- MEDIA…The media is also a target audience for safety communication!

The way safety information is communicated through the media will influence the public perception

Study and Program Oversight

Organised data collection

Solicited reports (classified as study reports + causality assessment)

- **Clinical** - clinical trials, non interventional studies including non-interventional post-authorisation safety studies
- **Marketing** - Market Research Programs, Patient Support Programs

- Local activities related to ongoing studies and programs can potentially trigger receipt of safety information
- One of the key responsibilities of the Local Safety Responsible is safety oversight of these activities
- Safety relevant activities may be outsourced to service provider (e.g.CRO) - appropriate reporting processes should be set up

Aggregate Reports

- Periodic Safety Update Reports (PSURs)/ Periodic Benefit-Risk Evaluation Rep

(PBRERs)

- Development Safety Update Reports (DSURs)
- Six Monthly Suspected Unexpected Serious Adverse Reactions Line Listing (SSI

Each report must be compiled, reviewed and distributed to the required Regulatory Authorities according to a schedule.

The marketing authorisation holder should **continuously evaluate** whether any re of the reference product information/reference safety information is needed wh new safety information is obtained during the reporting interval and ensure th changes made over the interval are described in PSUR section 4 (“Changes to t reference safety information”) and where relevant, discussed in PSUR section (“Signal and risk evaluation”).

PV Quality

- **Quality is the way of we do things. Maintain the high quality standards.**
- Safety Quality Management system should be in a place
- It is necessary to establish responsibilities and procedures to control

and enhance Drug Safety processes in order to maintain compliance.

Think about…

Inspection Readiness (keep up to date CV, job description, training records)

Pharmacovigilance Business Continuity Management Plan (PV BCM Plan)

-regulatory (EMA) requirement to train a → n

Incident

PV Agreements

- Marketing Authorization Holder (MAH) for its products has the responsibilit all Adverse Event (AE) reports, including those which arise from commercial Arrangements (e.g. Distribution Agreement, Co-Promotion Agreement, License and Supply Agreement…)

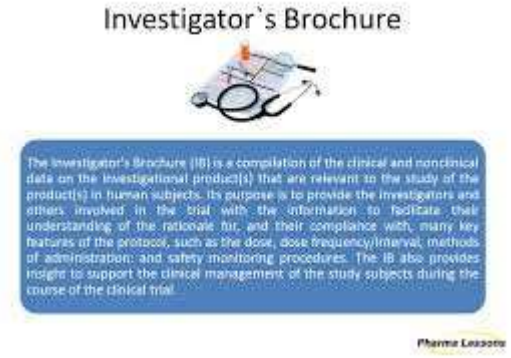
- The Pharmacovigilance activities documented in the **Pharmacovigilance Agreem** enables the Company to meet its worldwide regulatory safety reporting obligati Monitor/optimize the safety risk management of its products.

Labeling and PV Commitments

- **Labels:**

- Local implementation of safety related Core Data Sheet changes and safety sections
  of updated local labels prior to submission to the Regulatory Authority
- Investigator Brochure (IB) for clinical trials (The CDS is reviewed and updated periodically in ~~line~~ with IB updates)

Tra rma a tion



PV Commitments

- The **PV commitments** are any commitments made to Regulatory Authorities regarding the collection and submission of benefit and/or safety data/information that can have an impact on the benefit-risk balance of the marketed product in the licensed indication, beyond the obligation for spontaneous reporting of adverse events, and the periodic reporting of safety data defined by regulatory requirements.

- Marketing Authorization Holders are required to **continuously monitor** th commitments and ensure adherence.

- **Evidence** of the continuous monitoring of PV commitment activity must be provided in the Pharmacovigilance System Master File (PSMF).

Pharmacovigilance System Master File (PSMF)

- Provides oversight and detailed description of the entire PV system
- Supports and documents compliance with PV requirements
- Comprehensive tool for regulatory authorities/inspectors to oversee the PV system

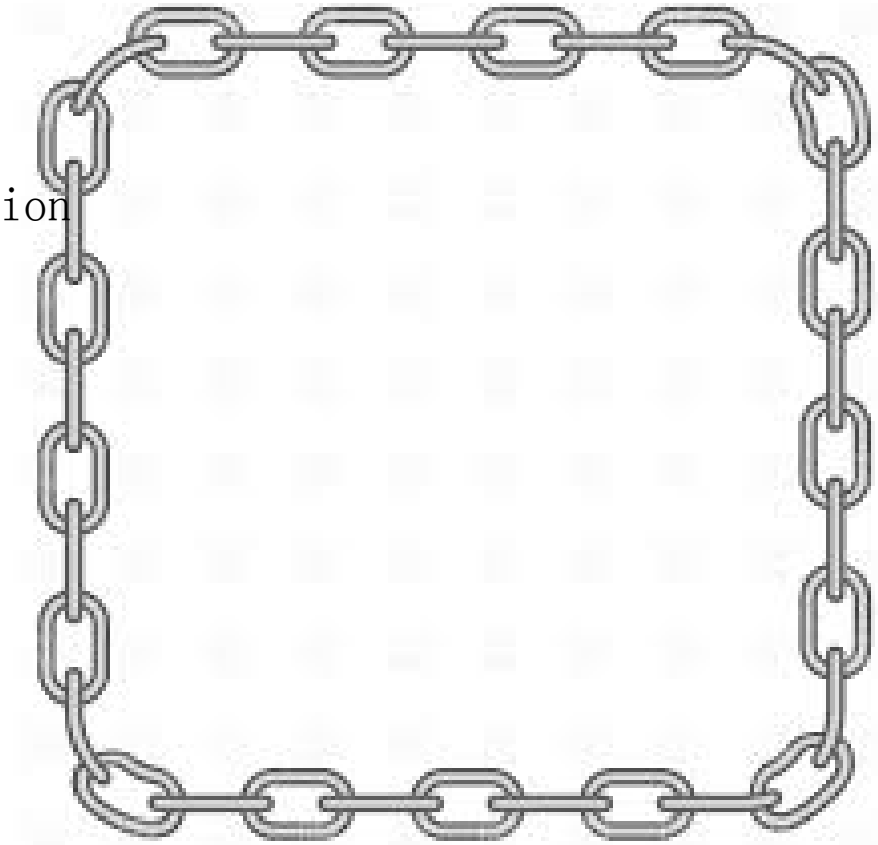
The regulators are demanding full transparency via the PSMF

Increased immediate external exposure = no time to react.

Therefore, ALL databases and lists must be up-to-date at all times!

Key words to keep PV chain strong

patients # adverse events



Protection of public heal

Education and training

Tracking

Communication

Quality Check

and Reconciliation

Compliance

Transparency

Cooperation

Doing now what patients need next

Sources

EMA webpages

Roche internal documents

Doing now what patients need next