SCOPE Joint Action
Work Package 8

Strengthening capabilities for benefit risk assessment

Jelena Ivanovic - AIFA

Stakeholder Event

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B/R assessment in PV

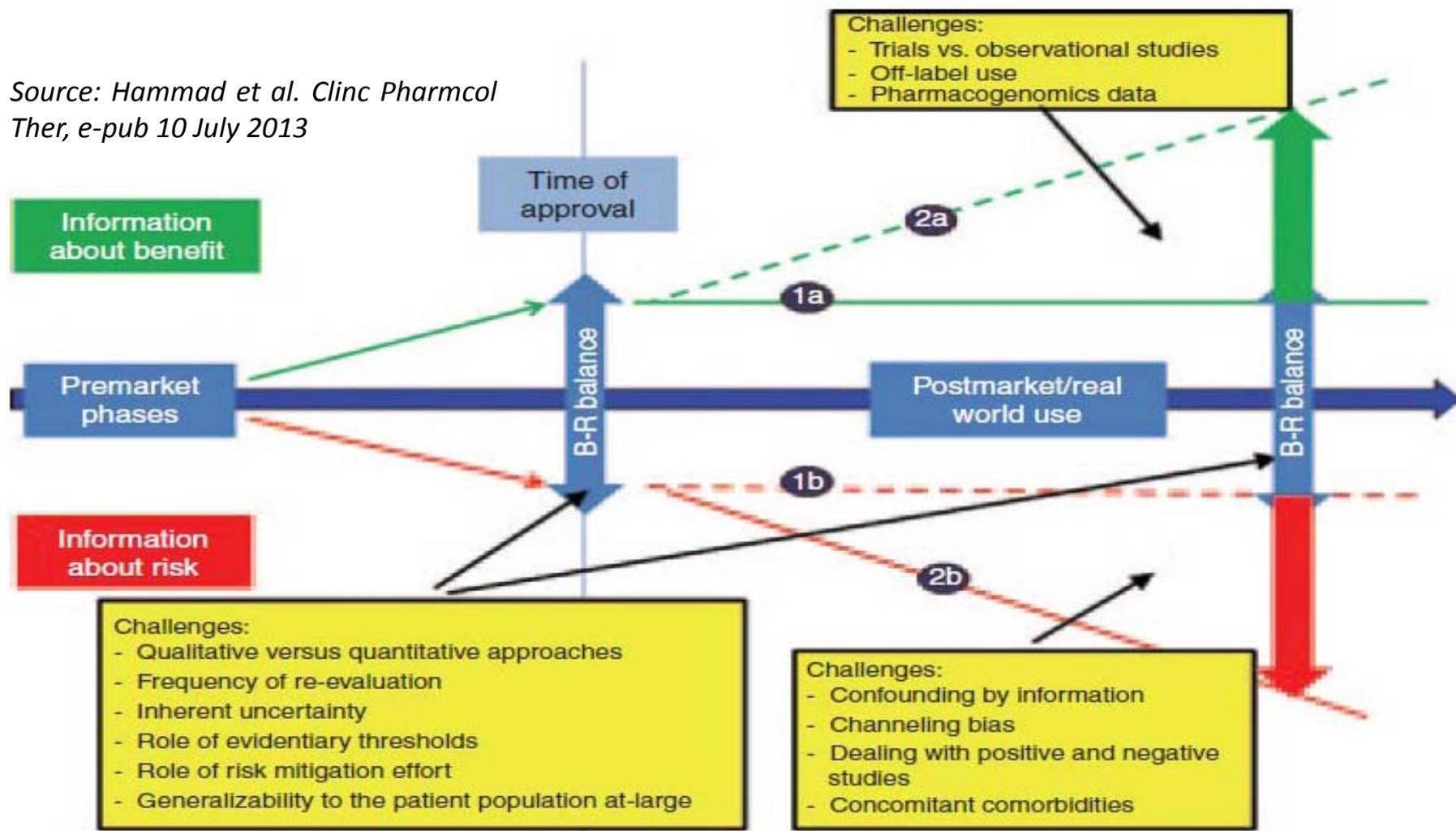"The dangers of life are infinite, and among them is safety."
-- *Goethe*

- B/R assessment in PV is a **complex task**;

- It takes into account **the extensive evidence of safety and effectiveness** as well as **many other factors** affecting the B/R assessment (e.g the nature and severity of the condition, the drug is intended to treat or prevent, the benefits and risks of other available therapies, any risk management tools that might be necessary to ensure that the benefits of the drug outweigh its risks etc.).

- The assessment involves both **quantitative analyses and a subjective qualitative weighing of the evidence**.

Lifecycle of benefit and risk information

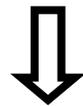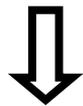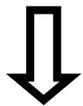*Source: Hammad et al. Clinc Pharmcol Ther, e-pub 10 July 2013*

The main goals of WP8

WP8 aims :

- to collect **information on methods and processes for PV assessments** and deliver a report on good practices useful for NCAs in operating PV effectively and to support the PRAC in its work;

- **to explore competency and useful alternative data sources** in the context of assessment of different PV procedures (RMPs and PASS, PSURs and referrals);

- **to support a competency framework** and, in the context of WP8 topics recommendations, **to promote consistency** in the B/R assessment throughout the lifecycle;

- to identify and **develop appropriate training materials**, based on the responses of all NCAs to the surveys and other data/information, to assist NCAs to develop their processes and to achieve improved effectiveness and competence.

WP8: Topics

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Lifecycle Pharmacovigilance - Lead Country: IT(AIFA)

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Coordination (IT lead) AC: ES, GR, IE, NL, NO, SE, UK.

Topic 1 (IT lead) AC: ES, GR, IE, NL, NO, SE, UK	Topic 2 (NO lead) AC: ES, GR, IE, IT, SE + PT, UK	Topic 3 (SE lead) AC: SE, IT, NO + UK, ES	Topic 4 (IT lead) AC: IE, SE, UK + ES, PT	Topic 5 (IT lead) AC: IE, UK + PT, ES, NO
Identification of available data sources outside of spontaneous reports	RMP assessment	Methodological approach for PASS assessment	Benefit/risk assessment of PSUR/PSURs and referrals	Competency

AC: Active contributors

The WP8 work plan and flow

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Stepwise approach:

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Questionnaires/survy
        ↓
Repors
(ESR and Topic reports)
        ↓
Topic Recommendations
        ↓
Training materials and
WP8 training
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Step 1: Development of **WP8 planner** and **questionnaires**

Step 2: Exploration of current situation among NCAs (assessment approaches as part of the medicines review process)

Step 3: Description of current situation among NCAs; **identification of challenges, a good practices and useful documents** (elaboration and dissemination in SCOPE)

Step 4: Development of WP8 recommendations to be used in the later training package for assessors to support consistency in evaluation of B/R of medicines in post-marketing setting

Step 5: Delivery of WP8 training materials and training for PV assessors to support consistency in PV procedures assessment

WP8: Key survey findings
Topic 1 - ADSs

- 70%of NCAs use ADSs during B/R assessment procedures;
- Registries and healthcare databases useful because based on population exposure or prescription/consumption data;
- The standard PV tools - WHO (Vigibase and Vigimine) and EMA (Eudravigilance, eRMR, etc.) and pre- and post- authorization data (DSURs and PSURs, PASS/PAES), often consulted during the assessment.
- ADSs are considered useful for detecting new ADRs, serious ADRs with low frequency and previously not studied DDIs;

- The selection of ADSs to be used during a B/R assessment is based on its:
  - ✓ accessibility
  - ✓ the possibility to analyze a large population exposed
  - ✓ the applicability of the data to the questions being explored in the assessment;

- Examples of Good Experience in use of ADSs in EU has been described:
  - ✓ Independent data sources of use in PV - the Spanish experience
  - ✓ Good experiences with an alternative data source: The UK
  - ✓ Italian Drug-Product Registries

WP8: Key survey findings
Topic 2 - RMPs

The survey reflected the current practice of assessment of RMPs with focus on challenges, possible solutions and good assessment practices.

- An organisation with **competent assessors and collaboration** with pre-clinical/clinical assessors are key elements;
- Providing **continuous training of assessors** is considered essential;
- **Limitation in human resources** has been identified as the major challenge;
- **Easy access to experts** within statistics/(pharmaco)epidemiology is of importance;
- The GVP Module V is used as the basic guidance for the assessment of RMPs in addition to guiding text in the assessment report templates;
- The survey identified some **areas where more guidance is needed**:
    - what risks are important enough to be included in the RMP, when additional PhV/studies are needed, when additional RMMs are needed;
    - criteria for removing safety concerns (and additional RMMs) from the RMP; during the products lifecycle should be developed within the European network;
    - assessment of the need for PAES;
    - the evaluation of study designs to document the effectiveness of additional RMMs.

The survey has helped to identify useful hints and tips for the assessment of the RMP.

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Present methods and processes in NCAs for the assessment of PASS protocols

- Out of 25 responders, 21 (84%) with **experience in evaluating PASS protocols**.
- **Joint assessment** considered to be important ;
- PV assessors in **collaboration** with clinical and pharmaco-epidemiology assessors are mainly involved;
- About half of the NCAs have access to **epidemiologic support**;
- 20/24 (83%) NCAs reported that a general epidemiological support should be available;
- 15/25 (60%) of the NCAs have some form of **a Quality System** which most commonly includes assessors meetings to discuss a draft assessment report;
- 14 NCAs generally accept proposed time tables and 5 NCAs commented that the time tables were too short especially for MS to comment;
- **Methods to support the assessor to adhere to time lines** involve internal deadlines and reminders, particularly for imposed PASS.

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Methods for the prioritisation and evaluation of PASS protocols

The approaches for the prioritisation and evaluation of PASS protocols and reports varied among the NCAs.

- Only 4 NCAs try to comment all PASS protocols and the remaining NCAs have some form of prioritisation to select when to comment;

- Different aspects for prioritisation were mentioned, e.g if the PASS were conducted nationally, if the PASS was imposed or the availability of expertise.

The NCA's experiences for specific assessors training

- The NCAs have identified several **training programs** and provided details of the courses and comments regarding suitability. Summarized in Annex II of WP8 Topic 5.

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Description of good practice and core skills required for successful evaluation

• **Comparison with other study protocols/reports** was the most frequently reported method to assist assessment;

• The NCAs use **GVP module VIII** as a guideline and half of the NCAs use EnCEPP's checklist and guideline;

• The mainstay in training is **senior PV assessors** acting as mentors;

• Additional training is most frequently provided on an ad-hoc and individual basis;

• Only a small number of NCAs mentioned some form of regular training program for new employees and/or assessors in this field;

• **The most reported challenges** identified by the NCAs were **complex study designs** followed by **the assessment of feasibility and promotional aspects**.

The survey has helped to identify useful hints and tips for the assessment of the PASS.

Organization and practices for the B/R evaluation

- **Internal deadlines, reminders** at set time points and **prioritization** identified as the most useful to deliver assessment reports according to timelines;

- **A meetings, TCs and close collaboration among NCA's** assessment team and EMA could further improve the consistency of the assessment;

- **A coordinator at national level** could have a key linking role in this process, together with EMA PM and PA;

- **A dedicated office or Press officer** in each NCA plays important role in the successful management of external expectations and reputational risk;

- Half of NCAs regularly or sometimes **seek advice from advisory board** or working group for achievement of the final NCA's position on B/R evaluation.

Organization and practices for the B/R evaluation

- 13 of 24 (54%) of the NCAs have **an internal quality system** (e.g. SOP, internal guide) for B/R assessment in context of PSUR assessment with reference to GVP module VII.

- For the referrals 74% of participating NCAs **do not have a formal internal guide** (e.g. SOP) which provides the more structured guidance for assessors.

- 21 of 24 NCAs, (87%) considers different factors when assessing these submission requirements for the PSUR cycle .

- The attention is particularly focused on **products with limited safety information** available and on **products with numerous and/or significant signals** emerged.

The useful tools to successfully carry out B/R assessments

- The availability of practical **guidelines/ checklists/"hint and tips"** for facilitation of the assessment was considered beneficial by NCAs.

- 2 NCAs provided in the survey **a specific practical guidance documents** to facilitate assessment :
  - a checklist providing the simple and clear instructions to be followed during the assessment process.
  - a "hints and tips" document as a guidance to facilitate programming and organisation of the work in the context of referrals.

- A positive effects of:
  - planning and "brain storming" meetings,
  - EMA template guidance texts,
  - internal "questions and answers" process for B/R assessment in PSUR/PSUSA and referrals have been identified in the survey.

- Some **possible challenges** during the PSUR/PSUSA and referral procedures have been identified and the full list is provided in the Annex 2 of the Topic 4 report.

WP8: Key survey findings
Topic 5 – Competency

Core assessor skills required for PV procedures assessment

- The **heterogeneity of requirements for assessors' professional profile** is one of the principal characteristics of the system which has emerged from the survey;

- The most **commonly reported criteria** for Junior assessor profile are:
    - university degree in biomedical sciences,
    - working experience in specific field,
    - high level knowledge of English
    - ability to work in a team,
    - ability to manage own workload and to adhere to proposed timelines,
    - ability to perform critical analysis of scientific research findings and literature,
    - basic knowledge of regulatory procedures,
    - adequate knowledge and use of computer applications,
    - obligatory training (including "on the job" training);

- Few replies on **the compulsory expertise and experience level for Senior Assessor** were received;

- Two examples of **criteria for definition of a Senior Assessor profile** were identified in the survey that could help NCAs to address this issue if necessary.

WP8: Key survey findings
Topic 5 – Competency

Competency levels and types of organization

- Most NCAs consider **a team assessment as essential** for evaluating B/R in PV procedures
- The appropriate **selection process and management of expert databases** could play an important role in achievement of the specific expertise. With regard to this issue, practices adopted in some NCAs were identified in the survey.
- Almost all NCAs have a quality system in place (e.g. **mentoring system, introduction program , obligatory trainings and/or sharing of experiences opportunities**) aimed to ensure a good level of expertise for newly employed assessors.

Training courses and literature recommended by NCAs

- **A trainings with different aims and levels at national and international (EU) level** are accessible training framework for different types of assessors.

Concept paper on Exchange program

- **The exchange program for assessors** was recognized by all NCAs as a valuable tool for the promotion of close collaboration, exchange of information and harmonization of effective standards for PV procedures evaluation (assessments).

WP8: Key survey findings

Some challenges that could influence the interpretation of the survey results:

- **not all European NCAs** have been participating **in SCOPE project**, thus figures reported in the reports reflect the current situation in SCOPE participating countries;

- not for all questions included in the WP8 survey was obtained the maximum **replaying rate**;

- the potentially **different interpretation of terminology and/or survey questions** and the fact that it was decided to not have a questionnaire with compulsory questions may influence the possibility to fully correlate obtained answers;

- **the national specific contexts**, for example the direct experience or not in some PV procedures , the responsibilities of the authorities as well as resources and priorities may induce uncertainties in generalization of the results.

WP8: Recommendations

A common format for recomendations from WP8 topics was developed including "Hints and tips" for different PV procedures (RMPs, PASS, PSUR/PSUSA and referrals)

- "**Hints and tips"** are not intended as a guidelines and **do not replace the existing guidance and requirements detailed elsewhere**, but written to share experience of the EU PV network and offer **practical advice on some aspects of assessment** and the drafting of Assessment Reports for assessors.

- **Assessors need to be familiar with the relevant legislation and guidelines** and are referred to these for formal guidance.

- They are:
    - **intended as a Reflection Papers** and derived from the experience and advice of assessors working in NCAs at both junior and senior level;

    - **a living documents**, subject to updates whenever new elements are considered to require integration.

WP8: Recommendations – work in progress

Topic 1 ADSs
- A list of ADSs with a description of their applicability and main characteristics.
- A separate section for the useful experience, described in ES, IT and UK.

Topic 2 RMP - "Hints and tips" on RMP Input on aspects concerning: • Organisation • Processes • Assessment of the Safety Specifications	• PV Plan • Risk minimisation Plan • Effectiveness of RMMs • Re-assessment of RMPs

Topic 3 PASS - "Hints and tips" on PASS
- Characterization of the methods to evaluate PASS and identification of MSs that are building a functional procedure in order to identify relevant issues to focus on.
- A future collaboration between NCA's who have come far in the PASS assessments and NCA's who just start their journey, perhaps in terms of alliances between NCA's.
- Future areas to consider e.g. central epidemiological advisory service and storage of PASS.

Topic 4 PSUR/PSUSA and referrals - "Hints and tips"

• to facilitate the work in the context of referrals and PSUR/PSUSA assessments will be developed and promoted in WP8 training program.

Topic 5 Competency

• Good practice examples concerning description of core assessor' skills required for PV assessments.

• Training courses and literature recommended by NCAs as useful for promotion of consistency in PV procedures assessment practices.

• Concept Paper on Assessors Exchange program - to establish the grounds for a sustainable program of secondment for European PV assessors enabling the exchange of experience and knowledge and facilitate an on-the-job training framework.

WP8: Deliverables

Topic	Deliverable	Time frame	AC
1	Catalogue of ADSs including description of NCAs examples	Completed - June 2015	IT, ES UK
2	"Hints & tips" on RMP	1 st draft June 2015 – 2 nd draft September 2015; Adoption in November 2015, Final 1st Q 2016	NO,IE, UK,PT, IT
3	"Hints & tips" on PASS	1 st draft avaited in October 2015; Adoption in November – Dicember 2015, Final 1st Q 2016	SE,UK,ES ,IT
4	"Hints & tips " on referral "Hints & tips " on PSUR/PSUSA	1 st draft July 2015; Adoption in November 2015; Final 1st Q 2016	IE, UK, IT, PT, ES
5	List of useful trainings and literature Concept paper on assessors exchange program	Completed – June 2015 1° draft July 2015; Adoption in November 2015; Final 1st Q 2016	IT ES, IT,PT,NO
All	**Report** **Final deliverable: WP8 training materials and FtoF workshop/training and webinar**	Completed - June 2015 3 rd Q 2016	All

WP8: Planned work

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www.scopejointaction.eu

Work on WP8 recommendations and deliverables

Topic Leads: General part of racommendations

Drafting Groups: TL + AC
Specific part of recommendations concerning supporting documents/practical guidance for assessors, concept paper etc.

Definition of WP8 training/workshop content and materials

- format
- package
- materials
- speakers

Common actions at SCOPE level

Linkage

Training/workshop logistics and delivery

Publication and disemination of results

WP8 Team

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Thank you for your attention!!

CONTACTS:

Jelena Ivanovic

Italian Medicines Agency –AIFA

Via del Tritone 181 - 00187 Rome

Phone: +39 0659784437

E-mail: j.ivanovic@aifa.gov.it