

# Post-authorisation safety studies and the EU PAS Register

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# Content of the presentation

- 1. PASS: definition and objectives (a reminder)
- 2. Obligations and recommendations
- 3. The EU PAS Register
- 4. Guidance for PASS protocol submission

#### 1. Definition and objectives



# Post-authorisation safety study: definition

Any study relating to an authorised medicinal product conducted with the aim of identifying, characterising or quantifying a safety hazard, confirming the safety profile of the medicinal product, or of measuring the effectiveness of risk management measures.

#### 1. Definition and objectives



# Objectives of a PASS:

- to quantify potential or identified risks
- to evaluate risks of a medicinal product used in patient populations for which safety information is limited or missing (eg pregnant women, specific age groups, patients with renal or hepatic impairment)
- to provide evidence about the absence of a risk
- to assess patterns of drug utilisation that add knowledge on the safety of the medicinal product (eg indications, dosage, co-medication, medication errors)
- to measure the effectiveness of a risk minimisation activity.

#### 1. Definition and objectives



## PASS initiated, managed or financed by a MAH.

- Pursuant to an obligation imposed by a competent authority
  - as a condition to the granting of the marketing authorisation, or after the granting of a marketing authorisation if there are concerns about the risks of the authorised medicinal product
  - as part of a marketing authorisation granted under exceptional circumstances.

## Voluntarily

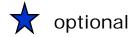
- > studies required in the risk management plan to investigate a safety concern or evaluate the effectiveness of risk minimisation activities
- any other PASS

# 2. Obligations and requirements



legal obligation

✓ recommended in the GVP



#### Management of study

|  | PASS with MAH involvement |                       |
|--|---------------------------|-----------------------|
|  | Imposed as an obligation  | Conducted voluntarily |
| Standard format of protocol and study report |                           | <b>✓</b>              |
| PRAC oversight                               |                           | (if in RMP)           |
| Registration of study in EU PAS register     |                           | ✓                     |
| Study not to promote medicinal product       |                           |                       |
| Restricted payment to HCP                    | _                         | _                     |
| Quality systems                              | _                         | <b>√</b>              |
| ENCePP methodological standards              | <b>✓</b>                  | ✓                     |
| ENCePP checklist for study protocol          | ✓                         | ✓                     |
| ENCePP CoC                                   | ✓                         | <b>√</b>              |
| ENCePP seal                                  | *                         | *                     |

# 2. Obligations and requirements





▲ legal obligation

recommended in the GVP

#### Reporting of study information

|  | PASS with MAH involvement |                       |
|--|---------------------------|-----------------------|
|  | Imposed as an obligation  | Conducted voluntarily |
| Protocol and progress reports to be submitted upon request to NCA of MS where study is conducted                         |                           |                       |
| Final report to be sent to the NCA of the MS where the study is conducted within 12 months of the end of data collection |                           |                       |
| Data generated in the study to be monitored  |                           |                       |
| Any information which may influence the B/R balance to be reported to NCAs of MS where the product is authorised         |                           |                       |
| Reporting of suspected adverse reactions in studies with primary data collection   |                           | _                     |
| Final manuscript of article to be transmitted to NCAs within 15 days after acceptance by journal editor                  | ✓                         | ✓                     |

#### 3. EU PAS Register



## Objectives

- transparency, exchange of information, peer review
- supports EMA to fulfil its obligation to make public protocols and results of PASS imposed as an obligation
- supports MS to ensure that the public is given important information on pharmacovigilance concerns
- repository of all non-interventional PAS conducted in the EU, irrespective of the source of funding and status of investigators (MAH, academia, regulatory or public health authorities,...)
- NOT to replace regulatory submission for imposed studies
- Accepted by MS as means for submitting information on studies conducted voluntarily (Annex 1 of GVP Module VIII)

#### 3. EU PAS Register



EU PAS Register to be developed as upgrade of ENCePP E-Register of studies and will include already registered studies, including ENCePP seal

# Transitional period:

- ENCePP E-Register of studies to be used
- Guide for study registration amended
- for MAH-sponsored non-interventional PASS required by a regulatory authority:
  - acknowledgment email sent by EMA to MAH
  - all Member States informed by EMA of the registration with: title, name of sponsor, countries, link to registry

#### 3. EU PAS Register



#### Impact on ENCePP

## "ENCePP study registry" will no longer exist

- confusion between "ENCePP study" and "study registered in ENCePP" will be avoided
- "ENCePP" trademark will refer to best methodological and ethical standards in pharmacoepidemiology
  - ENCePP Guide for methodological standards in pharmacoepidemiology
  - ENCePP Checklist for study protocols
  - ENCePP Code of conduct
  - ENCePP study seal

#### 4. Guidance for PASS protocol submission



## **Objectives**

- consistency in presentation and format of PASS protocols submitted by marketing authorisation holders
- provision of essential administrative information
- coverage of all important scientific aspects of a protocol

Legal obligation for imposed non-interventional PASS from 10 January 2013

Recommended for all other non-interventional PASS

http://www.ema.europa.eu/docs/en\_GB/document\_library/Other/2012/10/WC500133174.pdf

EMA → Regulatory → Human Medicines → Pharmacovigilance → Guidance



# Questions?