Pharmacovigilance in the EU: Practical Implementation across Member States

Michael Kaeding, Julia Schmälter, Christoph Klika
## Outline

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| (4) | Transposition of Directive 2010/84/EU |
| (5) | Method |
| (6) | ADR reporting systems in comparison |
| (7) | Perceived challenges and best-practices I-III |
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Research Aim

- Assessing the timely transposition and accurate implementation of Article 102 of Directive 2010/84/EU
  - Reporting of adverse drug reactions (ADRs) within the EU pharmacovigilance framework

- Contribution in many respects
  
  (1) Detailed account and comparison of ADR reporting systems across six member states
  
  (2) Identification and comparison of perceived challenges and best-practices
  
  (3) Recommendations on the necessary conditions for efficient pharmacovigilance systems
What are the major drivers impeding or incentivising practical implementation of ADR reporting (Art. 102, Directive 2010/84/EU) in EU member states?
Pharmacovigilance (Directive 2010/84/EU):

“Pharmacovigilance is the process and science of monitoring the safety of medicines and taking action to reduce the risks and increase the benefits of medicines.” (European Medicines Agency).

Reporting adverse drug reactions (Article 102):

- ADRs: noxious or unintended responses to a drug (WHO)
- Article 102 emphasizes the importance of reporting ADRs to the national competent authorities
Transposition of Directive 2010/84/EU
Method

- **In-depth comparison of ADR reporting** in:
  - Britain (ideal-type state healthcare system)
  - Finland (state-based mixed type)
  - Poland (state-based mixed type)
  - France (state-based mixed type)
  - Portugal (societal-based mixed type)
  - Germany (societal-based mixed type)

- **Document research**

- **Field research**

- **33 key informant interviews** (executives, healthcare professionals, industry, patients)
ADR reporting in Portugal

Regulatory Body
Ministério da Saúde (Health Ministry)

Executive Body

Regional Pharmacovigilance Centres
Norte (North)
Sul (South)
Centro (Centre)
Lisboa e Vale do Tejo (Lisbon and Tragus Valley)

INFARMED
Direção de Gestão do Risco de Medicamentos
(Directorate for Medicinal Risk Management)
Centro Nacional de Farmacovigilância
(National Centre for Pharmacovigilance)

Health Care Professionals
Doctors
Dentists
Pharmacists
Nurses
Medical Technicians

Patients
Pharmaceutical Industry
<table>
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<tr>
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<th>UK</th>
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<th>Poland</th>
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<tbody>
<tr>
<td><strong>System</strong></td>
<td>Centralized</td>
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<td><strong>System for</strong></td>
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<td><strong>Reporting by</strong></td>
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<td><strong>professionals</strong></td>
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<td><strong>(HCPs)</strong></td>
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<td><strong>industry</strong></td>
<td>Via Yellow Card Scheme to</td>
<td>Legally obliged in case of</td>
<td>To <strong>URPL</strong> (Office for</td>
<td>To regional centres, MAH,</td>
<td>To regional centres.</td>
<td>To MAH, associations, or</td>
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<td></td>
<td><strong>MHRA</strong> (Medicines &amp;</td>
<td>vaccines.</td>
<td>Registration of Medicinal</td>
<td><strong>ANSM</strong> (Agence</td>
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<td><strong>BfArM</strong> (Federal Inst. for Drugs and Medical Devices).</td>
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<td>Healthcare Products</td>
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<td>Products, Medical Devices</td>
<td>Nationale de Sécurité</td>
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<td>Regulatory Agency), or</td>
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<td>and Biocidal Products).</td>
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<td>Produits de Santé).</td>
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<td><strong>patients</strong></td>
<td>To MHRA.</td>
<td>To Fimea.</td>
<td>To <strong>URPL</strong>.</td>
<td>To ANSM.</td>
<td>To <strong>INFARMED</strong></td>
<td>Leg. obliged. To <strong>BfArM / PEI</strong>.</td>
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<td><strong>industry</strong></td>
<td>To MHRA, physician, MAH.</td>
<td>To Fimea, physician, MAH.</td>
<td>To <strong>URPL</strong>, physician, MAH.</td>
<td>To regional centres, ANSM,</td>
<td>To regional centres or HCPs.</td>
<td>To <strong>BfArM</strong>, PEI, HCP, industry.</td>
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<td>physician,MAH.</td>
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Underreporting as major challenge in all systems

- Quantity: recurrent and non-serious ADRs are rarely reported
- Quality: missing batch number, brand name, patient information

Reasons

- Lack of awareness
  - Education & training
  - Media activity
- Lack of time and personnel
- Insufficient infrastructure
  - IT-connectivity
  - Networking and cooperation
# Perceived challenges and best-practices II

<table>
<thead>
<tr>
<th>Awareness raising</th>
<th>UK</th>
<th>Finland</th>
<th>Poland</th>
<th>France</th>
<th>Portugal</th>
<th>Germany</th>
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<tbody>
<tr>
<td>Education</td>
<td>No priority in academic education. Not enough post-graduate trainings. MHRA offers free e-learning modules</td>
<td>Mandatory university curriculum. Fimea offers post-graduate trainings</td>
<td>No mandatory university courses. Limited post-graduate trainings. URPL offers trainings</td>
<td>MA degree</td>
<td>Older healthcare generations insufficiently educated. Regional centres offer trainings</td>
<td>Only part in pharmacy studies</td>
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<tr>
<td>Media</td>
<td>Facebook, Twitter, App, Newsletter</td>
<td>Facebook, Twitter, Youtube, Movies</td>
<td>Regional centres provide information</td>
<td>Regional centres provide information</td>
<td>Red and blue hand letters, App</td>
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<table>
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<tr>
<th>Resources</th>
<th>UK</th>
<th>Finland</th>
<th>Poland</th>
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<td>Lack of financial and human resources</td>
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<td>Depend on Ministry of Finance</td>
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<td><strong>IT connectivity</strong></td>
<td>UK</td>
<td>Soon integration of Yellow Card Scheme into clinical IT-systems. Duplication detection program.</td>
<td>FIMEA sends reports to companies via post. System complex and time consuming</td>
<td>IT-systems of physician &amp; pharmacist connected</td>
<td></td>
<td>IT-infrastructure not harmonized. Problem of duplication. Data protection</td>
</tr>
<tr>
<td><strong>Networking</strong></td>
<td>UK</td>
<td>Cooperation between MHRA and NHS. National Medication Safety Network</td>
<td></td>
<td>31 regional centres with close connection to HCPs, students and patients</td>
<td>Regional centres cooperate with universities. Active data collection</td>
<td>Consultancy centre in Berlin</td>
</tr>
</tbody>
</table>

**Perceived challenges and best-practices III**
Conclusion

- **ADR reporting is perceived as insufficient** in terms of information quantity and quality in all six countries
  - Particularly with regard to reporting batch numbers of biological medicines

- **Next steps**
  - Issue recommendations covering major shortcomings
    - awareness raising (media, education)
    - infrastructure (networking, IT-connectivity)
    - human and financial resources
Thank you for your attention!

Any questions?
ADR reporting in the UK

Secretory of State Health Ministers

Department of Health

Executive Agency

MHRA
Medicines & Healthcare products Regulatory Agency

Yellow Card Scheme

Database

Medication ADR-Reporting

Health Care Professionals

Patients

Pharmaceutical Industry

Transformed in an Individual Case Safety Report

Own sources

Advisory NDPB

Commission on Human Medicines
ADR reporting in Finland
ADR reporting in Poland

Regulatory Body
Ministerstwo Zdrowia
Ministry of Health

Executive Body

URPL
Office for Registration of Medicinal Products, Medical Devices and Biocidal Products
Unit for Pharmacovigilance

ADR reporting

Health Care Professionals
Doctors / Dentists
Pharmacists
Midwives
Nurses
Paramedics
Laboratory Technicians

Patients

Pharmaceutical Industry
Medicinal Product Manufacturers
Marketing Authorisation Holders
ADR reporting in France

Regulatory Body
Ministry for Health and Social Security

Executive Body

ANSM
(Agence Nationale de Sécurité de Médicament et des Produits de Santé – Agency for Drug Safety and Health Products)

Unité de Pharmacovigilance
Technical Committee

31 CRPV
(Centres Régionaux de Pharmacovigilance – Regional Centres for Pharmacovigilance)

Health Care Professionals
Doctors
Dentists
Pharmacists
Midwives

Patients

Pharmaceutical Industry

ADR reporting
ADR reporting in Portugal

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