The European Falsified Medicines Directive
Prof. Patrick Deboyser
EU Action Against Falsified Medicines

- Safety features
- Reinforcing the distribution chain
- Internet sales
- Active substances

Directive 2011/62/EU on falsified medicinal products
EU Action Against Falsified Medicines

Reinforcing the distribution chain

New/Updated GDP guidelines:
- For medicinal products (November 2013)
- For APIs (March 2015)

EudraGMDP
- EU database of medicinal product distributors

API distributors
- Mandatory registration with NCAs
Active substances

**EU Action Against Falsified Medicines**

APIs can only be imported into the EU if:
- Written confirmation on GMP for API; or
- Exporting country is "listed" by the Commission; or
- EU GMP certificate.

New requirements for API manufacturers:
- Registration of EU API manufacturers and importers;
- Audit by manufacturers of medicinal products;
- Inspections by NCAs;
- Legally binding GMP for APIs (based on ICH Q7)
EU Action Against Falsified Medicines

EU common logo for online pharmacies

- Since 1 July 2015, a EU common logo identifies all websites legally selling medicinal products in the EU
- Clicking the logo securely redirects to a list of authorised pharmacies in a given MS

Online pharmacies must be registered

- By the NCA of the Member State in which they are established

Awareness campaigns by MS to inform

- On the risks of buying online
- On the functioning of the common logo
EU Action Against Falsified Medicines

- **Safety features**
- **Unique identifier (UI)**
  - Code enabling:
    - the identification and
    - the authentication of a given pack.
- **Anti-tampering device (ATD)**
  - Device allowing the verification of whether a pack has been opened/tampered with.
Delegated Regulation 2016/161

- Lays down detailed rules for the safety features appearing on the packaging of medicinal products
- Applies as of 9th February 2019 in all MS.
- Packs on the market before February 2019 can stay on the market until their expiry date
- BE, EL and IT may defer the application by up to 6 years.
Regulation 2016/161 provides for:

- Technical characteristics of the UI
- Repositories system for the UI
- Verification of the safety features
- List of exceptions from bearing/not bearing the safety features

Regulation 2016/161 does not provide for:

- Technical options for the anti-tampering device
Scope: principles

- **Prescription medicines** for human use must bear the safety features.
- **Non-prescription medicines** for human use are exempted.

Scope: exceptions

- **Prescription medicines** exempted from the safety features: homeopathics, radiopharmaceuticals, ATMPs, medical gases, certain solutions, contrast media, allergy tests and allergens.
- **Non-prescription medicines** requested to bear the safety features: Omeprazole 20 or 40 mg (reported incidents of falsification)
## EU Action Against Falsified Medicines

### Safety features

### Unique Identifier (UI) : composition

- **Product code:**
  - ISO-compliant (ISO 15459)
  - < 50 characters
  - globally unique
  - issued by ISO-compliant coding agencies

- **Serial number** (max 20 characters; randomized)

- **Batch number**

- **Expiry date**

- Optional: national reimbursement or identification number

<table>
<thead>
<tr>
<th>Product code</th>
<th>Serial number</th>
<th>Batch number</th>
<th>Expiry date</th>
</tr>
</thead>
<tbody>
<tr>
<td>(01)09876543210982</td>
<td>(21)12345AZRQF1234567890</td>
<td>(10)A1C2E3G4I5</td>
<td>(17)032021</td>
</tr>
</tbody>
</table>
EU Action Against Falsified Medicines

Safety features

Unique Identifier (UI) : properties

- A unique code (UI) on each pack
- The UI is carried by a 2D barcode (Data Matrix ECC200)
- Human-readable format
- Minimum printing quality

PC: 09876543210982
SN: 12345AZRQF1234567890
NN: (optional)
Batch: A1C2E3G4I5
Expiry: 032021

Illustrative example – not binding
EU Action Against Falsified Medicines

Verification of the safety features (I)

- An end-to-end verification system – not a full track & trace system

- One end - Manufacturers/MAH:
  - UIs are printed on packs and uploaded in a secure repositories system.
  - ATDs are applied on packs.

- Other end – Pharmacies/hospitals:
  - UIs are systematically verified for authenticity and decommissioned at the time of supply to the public.
  - The integrity of the ATD is checked.
EU Action Against Falsified Medicines

Verification of the safety features (II)

- What happens in the middle of the chain?
- Risk-based verification by wholesalers, who verify the safety features when:
  - The product is not directly supplied from a manufacturing or marketing authorisation holder (or a person supplying on their behalf);
  - The product is returned by another wholesale distributor or a pharmacy.
EU Action Against Falsified Medicines

Verification of the safety features (III)

- End-to-end verification system
- Risk-based verifications
Verification of the safety features (IV)

- Member States **can exempt** certain persons from the obligations to verify/decommission:
  - Veterinarians, dentists, opticians, paramedics, nursing homes, etc. (full list in Article 23)
  - In this case the verification/decommissioning of the UI is performed by the wholesaler supplying those persons.

- Member States **cannot exempt pharmacies** nor healthcare institutions.
The Repositories system (I - Characteristics)

- **Main tasks:**
  - store the information on the legitimate UIs, and
  - allow the verification/decommissioning of UIs at any point of the supply chain.

- Physically located in the European Union.

- Established and managed by **stakeholders**.

- Supervised by **Member States**.

- It consists of:
  - a central information and data router (‘hub’), and
  - national or supranational repositories connected to the hub.

**Safety features**

EU Action Against Falsified Medicines
EU Action Against Falsified Medicines

Safety features

The Repositories system (II - Architecture)

- Architecture: a distributed system

Source: ESM/EMVO
The Repositories system (III - Access)

- The repositories system can be queried by verified users, i.e. users whose identity, role and legitimacy has been verified.
- National competent authorities (NCAs) can access the repositories system and the information contained therein for:
  - supervising the functioning of the repositories
  - investigating potential incidents of falsification;
  - reimbursement;
  - pharmacovigilance or pharmacoepidemiology.
EU Action Against Falsified Medicines

References


- Regulatory requirements: Implementation plans published by EMA and CMDh

Thank you!