Serialization in EU member states – Safety Features

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Legislation Overview
The Falsified Medicines Directive

DIRECTIVE 2011/62/EU OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 8 June 2011

- European response to the increase of falsified medicinal products detected in the Union
- Definition of falsified medicines
- Introduction of safety features for medicinal products
FALSIFIED MEDICINES

Falsified medicinal product - Any medicinal product with a false representation of:

(a) its identity, including its packaging and labeling, its name or its composition as regards any of the ingredients (including excipients) and the strength/dosage of those ingredients;

(b) its source, including its manufacturer, its country of manufacturing, its country of origin or its marketing authorization holder (MA); or

(c) its history, including the records and documents relating to the distribution channels used.

Unintentional quality defects or infringements of intellectual property rights aren’t included.
SAFETY FEATURES

- Several meetings between representatives of the MS were held

- A concept paper was submitted to public consultation (2011) to facilitate an impact assessment of the possible policy options and prepare the delegated act

- Several opinions were received (80):
  Regulatory Medicines Agencies
  European Federation of Pharmaceutical Industries and Associations
  European Generic Medicines Association
  National Associations of Pharmaceutical Industries
  National Associations of Generic Medicines
  Wholesale Distributors Associations
  Pharmacies Associations
  European Association of Hospital Pharmacies
  Pharmacetic Associations
  Organizations of norm standard systems (GS1, IFA)
  Stakeholders
Delegated Act/Regulation

- Definition of which medicines should have safety features
- Characteristics and Technical specifications of the Unique Identifier (UI)
- Defines how the verification of the UI is made
- Repository Systems
Safety features
SAFETY FEATURES


Safety Features

- verification of the authenticity of medicines
- identification of individual packs
- Acquire evidence of tampering
Which medicines should have safety features?

**Rule:** Medicinal products subject to prescription shall bear the safety features. 
[54.a) of the Directive]

All prescription medicines that shall not have safety features (risk assessment)

↓

White List

All non prescription medicines that must have safety features (falsification risk and history)

↓

Black List

Medicinal products to which the MS extended the scope of the safety features
White Lists – **Annex I of the Delegated Regulation**

a) Homeopathic Medicines  
b) Radionuclide Generators and precursors  
c) Kits  
d) Advanced Therapy Medicinal Products which contain or consist of tissues and cells  
e) Medicinal gases  
f) Solution for parenteral nutrition with ACT code B05BA  
g) Solutions affecting electrolyte balance ATC code B05BB  
h) Solutions producing osmotic diuresis ATC code B05BC  
i) Intravenous solution additives ATC code B05X  
j) Solvents and diluting agents  
k) Contrast media having ATC code V08  
l) Tests for allergic diseases ATC code V04CL  
m) Allergen extracts ATC code V01AA
Black Lists – Annex II of the Delegated Regulation

a) Omeprazole, gastro resistant Capsule, hard, 20 mg

a) Omeprazole, gastro resistant capsule, hard, 40 mg
Which medicines should have safety features?

Doesn't apply to:

a) Veterinary medicinal products

b) Medicines that doesn't have yet a marketing authorization (research and development trials).

c) Individual patients dose/pack (automated dose dispensing)
Safety Features

- Unique Identifier
- Anti tampering Device
Anti-tampering device

Safety feature that allows the verification of whether the packaging of a medicinal product has been tampered with.

The verification of the integrity of the anti-tampering device shows whether the packaging has been opened or altered since it left the manufacturer, thereby ensuring that the content of the packaging is authentic.

All characteristics and technical specifications of anti-tampering device is decided by the manufacturer

The Delegated Act doesn’t regulate the characteristics of this safety feature
Art. 5 nr 1 of the Delegate Regulation:
“Manufacturers shall encode the unique identifier in a two-Dimensional barcode”

Barcodes should be a machine readable Data Matrix, printed on a uniform, smooth and low reflecting surface
Unique Identifier

UI

Mandatory information

- Sequence of numeric or alphanumeric characters for each package (max. 20) determined by algorithm (Serial number)
- Name of the medicine, and common name, Pharmaceutical form, strength, pack size and pack type – max 50 (Product Code)
- National reimbursement number, or other national number that identifies the product
- Batch number and expiry date
Unique Identifier

Unique identifier
Human readable format
If possible, adjacent to the 2D codes

- Serial Number
- Product code
- National reimbursement number, or other national number that identifies the product

Exception: packages with less than 10 cm (sum of the 2 longest dimensions)

Font size: Guideline on the readability of the labelling and package leaflet of medicinal products for human use Eudralex – notice to applicant – volume 2C
Unique Identifier

Verification of the authenticity of the UI

Check the repository system

If active in the repository: It’s authentic

Who can do the verification? Manufacturers, wholesalers and persons that can sell medicines to the public
Unique Identifier

When to Verify the authenticity of the UI?

- Wholesaler
  - Returned medicines
  - Medicines proceeding from other wholesalers
Unique Identifier

When to Verify the UI?

Exceptions:

- Medicines proceeding from the manufacturer, MA Holder, or Wholesaler contracted to distribute medicines by the MA Holder, on his behalf (written contract);

- Medicines that changed ownership but remained in the physical possession of the same wholesaler;

- Medicines distributed in the same MS between warehouses of the same wholesaler.
Unique Identifier

When to Decommission the UI?

Wholesaler

- Returned medicines, which can’t come back to sealable stock
- Products to be sold outside EU
- Medicines to be destroyed
- Medicines requested by Authorities
- Medicines to be sold to prisons, dental practitioners, etc. – Art. 23.º
Unique Identifier

Persons that supply medicines to the public
Pharmacies, retailers, hospitals, etc.

- Verify the UI, when selling the medicine to the public
- If in a healthcare institution, verification can be made at any time, since physical possession, if there is no subsequent sale
- Connect to the repository system
- Decommission the UI of medicines that can not be returned
Unique Identifier

When to Verify the UI?

Exceptions:

- Free Samples

- If wholesalers have that obligation (art. 23rd)

- If MS decide to exempt a person authorized to supply a medicine in a healthcare institution, when:
  - The supplier is a wholesaler belonging to the same legal entity;
  - If the decommission is performed by the wholesaler;
  - No sale is made between the decommission and the supply to the healthcare institution;
  - The medicine is supplied to the public in that institution.
Unique Identifier

Can a Decommission be reversed?

Yes! If...

- The person reversing is covered by the same authorization and operates from the same premises
- The reversion does not happen more than 10 days after the decommission
- The pack is not expired
- The pack wasn't registered in the repositories as recalled, withdrawn, intended for destruction or stolen
- The product has not being supplied to the public
When the exceptions apply, the anti tampering device must me checked before supplying the medicine to the public.

When supplying part of pack (p.e. hospitals) the verification of safety features and decommission must be made when the pack is opened for the first time.

Falsification suspicion: obligation to report that suspicion to Authorities (manufactures, wholesalers, persons authorized to supply to the public)
Unique Identifier

Technical problems

People responsible for the verification and decommission must register the unique identifier (human readable format) by any suitable method and must make the verification as soon as possible/when the system is available (manual query of the system).

The supply to the public is suspended if there is a reason to believe that the packaging has been tampered with or the product is not authentic.

Other situations  National regulation is needed

If the UI is unreadable/damaged  the product shouldn't be supplied to the public
Repository Systems
Repositories System

The repositories system is where all the information on the safety features shall be contained, allowing the verification of the authenticity of medicines

Managed by EMVO
(European Medicines Verification Organisation)

European HUB

National Repositories or Supranational Repositories
Repositories System

1) Data elements of the UI
2) Product code
3) ID of the product (name, pack size, etc.)
4) Member State(s) to be placed
5) Code of entry in the national database (IA)
6) Name and address of manufacturer
7) Name and address of MA Holder
8) List of wholesalers designated to distribute the medicines in the behalf of the MA Holder
Repositories System

- Physically located in the EU
- Managed by a non-profit legal entity established in the EU by manufacturers and MA holders
- Shall allow fully interoperability with other repositories and reliable electronic identification and authentication of individual packs
- Shall allow the transfer and data exchange between software's used by wholesalers or persons that sell medicines to the public
- Shall allow wholesalers or persons that sell medicines to the public to query the repository and the response shall be lower than 300 milliseconds in 95% of the queries
- Audit trail of all operations concerning a UI at least until a year after the expiry date or 5 years after the released for sale or distribution
- Guarantee of data safety and direct access from wholesalers and persons that sell medicines to the public and Authorities
Repositories System

Access granted after verification of the legitimacy of the entity

Entities should have access to the data generated with their interaction with the repositories and information about the status of the UI

The legal entity managing the repository has no access to it except for investigation of potential falsification
Authorities must make the following information available:

a) Products that shall bear safety features;
b) Products that shall have UI (extended scope)
c) Products that shall have anti tampering device (extended scope)

Authorities must supervise the functioning of any repository located in their territory
Repositories System

Products recalled, withdrawn, stolen

The person responsible to place those medicines in the market must:

- Decommission the UI
- Inform the repositories about the event
Challenges for the future
Main Challenges

1) Data security issues
2) Data access issues
3) IT adaptation issues and costs
4) More GMP, distribution and supply requirements to inspect and supervise
5) Inspectors training in UI and repository database, and info analysis
6) Asymmetries between countries may imply more costs and different requirements
7) More cooperation between countries and between Authorities and national stakeholders and entities
Thank you for your attention

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Regulatory requirements of the packaging

Implementation plan for centralized medicines:


National requirements:

Unique Identifier

Every operation performed on the unique identifier must be recorded and kept by the manufacturers for at least one year after the expiry date or five years after the pack has been released for sale or distribution, which ever is longer, and shall provide those records to competent authorities, if needed.
COUNTERFEIT MEDICINES

Medicines that present infringements regarding intellectual property rights.
• Counterfeit or reproduction of a registered brand without their owner consent;
• Undue use of a registered brand
• Imitation, with the intent to take advantage of the established brand or worth of the imitated product.

ILLEGAL MEDICINES

All falsified and counterfeit medicines are illegal, but not all illegal medicines are falsified.

Medicines that are authorized in another country but don't have a Marketing Authorization in Portugal are considered illegal.
Is a printing quality of 1.5 according to ISO/IEC 15415 mandatory?

No!

Manufacturers are required to use a printing quality which ensures the accurate readability of the Data Matrix throughout the supply chain until at least one year after the expiry date of the pack or five years after the pack has been released for sale or distribution in accordance with Article 51(3) of Directive 2001/83/EC, whichever is the longer period.

The use of a printing quality of 1.5 or higher gives a presumption of conformity, i.e. manufactures using a printing quality of 1.5 or higher will be presumed to have fulfilled the requirement mentioned in the first paragraph without need to prove that it is actually the case.

If a printing quality lower than 1.5 is used, manufacturers may be asked to prove that requirements mentioned above are met.