Verification of Medicinal Products in Europe
An EIPG Perspective

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The Falsified Medicines Directive

- **Objective**: the prevention of entry into the legal supply chain of falsified medicinal products
- **Falsified medicinal product**: Any medicinal product with a false representation of:
  - its ***identity***, including its packaging and labelling, its name or its composition as regards any of the ingredients including excipients and the strength of those ingredients
  - its ***source***, including its manufacturer, its country of manufacturing, its country of origin or its marketing authorisation holder
  - its ***history***, including the records and documents relating to the distribution channels used

The Falsified Medicines Directive

- **Safety features** (unique identifier, UI) enabling wholesale distributors and persons authorised or entitled to supply medicinal products to the public to
  - verify the authenticity of the medicinal product, and
  - identify individual packs
- **Device** allowing verification of whether the outer packaging has been tampered with.
- The **Qualified Person** shall ensure that the safety features have been affixed on the packaging.

The Falsified Medicines Directive

- **Medicinal products**
  - Subject to prescription shall bear the safety features, unless they have been included in the “white list”
  - Not subject to prescription **shall not** bear the safety features, unless they have been included in the “black list”

The Delegated Act

- **Delegated Act** to set out
  - The characteristics and technical specifications of the UI
  - "Black list" and "White list", and procedures for notification
  - Modalities for verification of the safety features
  - Provisions on the establishment, management and accessibility of the repositories system in which information on the safety features shall be contained

The Delegated Act

The Delegated Act

- Adopted by the European Commission on 2nd October 2015
- Published in the *Official Journal of the European Union* on the 9th February, 2016.
- Enters into force 29th February
- Applies from 9th February, 2019
  - Belgium, Italy, Greece 9th February 2025
  - Fade-out phase to expiry of products

The Unique Identifier

- The **Unique Identifier** shall consist of
  - 'product code' (identifying name, common name, form, strength, pack size, pack type, maximum 50 characters, globally unique)
  - 'serial number' (numeric/alphanumeric, maximum 20 characters, randomised, less than 1 in 10,000 chance of guessing)
  - batch number
  - expiry date
  - national reimbursement number, if required by MS
- Combination of product code and serial number shall be unique to a given pack until at least one year after expiry or 3 years after QP release, whichever is longer

The Unique Identifier

- The unique identifier shall be encoded in a 2-D barcode
  - Machine-readable datamatrix (ISO/IEC 16022:2006) with internationally recognised coding scheme (ISO/IEC 15418:2009)
  - Product code, serial number, national reimbursement number shall also be printed in human-readable format as long as sum of two longest dimension is > 10 cm.
  - Batch number and expiry date are already printed under Labelling and Package Leaflet in the Directive.

The Manufacturers

- Place on the packaging of a medicinal product a unique identifier, encoded in a 2-D barcode
- Evaluate the quality of printing of the datamatrix
- Establish minimum quality of printing that ensures accurate readability throughout the supply chain till one year after expiry or five years after release, whichever is longer.
- Verify that the 2-D barcode is compliant, readable and contains correct information

The Manufacturers

- Keep records of every operation with or on the UI for at least one year after expiry or five years after release, whichever is longer

- The MAH shall ensure that the information is uploaded to the repositories system by the manufacturer **before the medicinal product is released for sale or distribution** (shared packs!)

Qualified Person responsibilities: Annex 16 coming into operation on the 15th April 2016 has no information in respect of the Delegated Act, the Unique Identifier or the Repositories System

The Wholesale Dealers

- Verification of the authenticity of the UI when
  - medicinal products are returned by persons authorised or entitled to supply medicinal products to the public or by another wholesaler

"Medicinal products which have left the premises of the distributor should only be returned to saleable stock if all of the following are confirmed:

(v) the distributor has reasonable evidence that the product was supplied to that customer (via copies of the original delivery note or by referencing invoice numbers, etc.) and the batch number for products bearing the safety features is known, and that there is no reason to believe that the product has been falsified."

The Wholesale Dealers

- Verification of the authenticity of the UI when

"Appropriate qualification and approval of suppliers, should be performed prior to any procurement of medicinal products. This should be controlled by a procedure and the results documented and periodically rechecked."

  - medicinal products are received from a wholesaler who is neither the manufacturer nor the wholesaler holding the marketing authorisation nor a wholesaler who is designated by the marketing authorisation holder, by means of a written contract, to store and distribute the products covered by his marketing authorisation on his behalf

The Wholesale Dealers

- Verification of the authenticity of the UI when
  - medicinal products are returned by persons
  - medicinal products are received from a wholesaler who is neither the manufacturer nor the wholesaler
  - to store and distribute the products covered by his marketing authorisation on his behalf

"Each repository in the repositories system… shall maintain a complete record ('audit trail') of all operations concerning a unique identifier, of the users performing those operations and the nature of the operations;"

"Documentation comprises all written procedures, instructions, contracts, records and data, in paper or in electronic form. Documentation should be readily available/retrievable."

The Wholesale Dealers

- Verification is not required when
  - medicinal product changes ownership but remains in the physical possession of the same wholesaler
  - medicinal product is distributed within the territory of a Member State between two warehouses belonging to the same wholesaler or the same legal entity, and no sale takes place

The Wholesale Dealers

- Verification and decommissioning of the UI for
  - products to be distributed outside the EU
  - products returned by persons authorised or entitled to supply medicinal products to the public or another wholesaler and cannot be returned to saleable stock
  - products intended for destruction
  - products which, while in physical possession, are requested as a sample by competent authorities
  - products distributed to special persons or institutions, according to national legislation

The Falsified Medicines Directive

- **Medicinal products**
  - Subject to prescription shall bear the safety features, unless they have been included in the "white list"
  - Not subject to prescription **shall not** bear the safety features, unless they have been included in the "black list"

"Once Regulation (EU) No 2016/161 applies, manufacturers cannot place the safety features on medicinal products not required to bear the safety features, unless the Member States have extended the scope of application of the unique identifier or of the anti-tampering device to those medicinal products in accordance with Article 54a(5) of Directive 2001/83/EC."

The Falsified Medicines Directive

- **Medicinal products**
  - Subject to prescription shall bear the safety features, unless they have been included in the "white list"
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"Medicinal products which have left the premises of the distributor should only be returned to saleable stock if all of the following are confirmed:

(i) the medicinal products are in their **unopened** and undamaged secondary packaging and are in good condition;"

The Falsified Medicines Directive

earch Chicago Tribune Sept. 1, 1982

5 deaths tied to pills

Fear killer put cyanide in Tylenol

By Jack Houston
and Jean Latz Griffin

CYANIDE-FILLED capsules of Extra-Strength Tylenol were blamed for the deaths of three persons in suburban Cook County, the critical illness of another, and probably the deaths of two Du Page County women Thursday.

As the toll rose, the federal Food and Drug Administration warned persons throughout the country against use of the popular pain reliever in capsule form, broadening an earlier warning.

And in Du Page County, Dr. James P. Paulissen, director of the health department there, warned against taking any form of Tylenol. "Although only Extra-Strength Tylenol has been indicted, prudence dictates that all forms of Tylenol are possible suspects," he said.

Tylenol, according to one business community expert, is the biggest nonprescription painkiller in the U.S., with approximately $400 million in sales this year.

THE COOK COUNTY medical examiner's office said the deaths of three persons in Arlington Heights and Elk Grove Village are being treated as homicides because the capsules in bottles of the product they used had apparently been tampered with.

In Du Page County, Deputy Coroner Peter Seikmann said one victim was found to have had Tylenol in her home and an inspection of the capsules found four containing cyanide. Cyanide was found late Thursday in five of 10 Extra-Strength Tylenol capsules found in the

Tribune photo by Charles Osgood

Samples taken from Tylenol capsules connected with one of the deaths were analyzed by Cook County doctors. The chunky sample [right] contained cyanide, while the one on the left contained only normal chemicals associated with the product.

Full coverage

- The little red-and-white pills have become a deadly game of cyanide-roulette, officials say. Sec. 2, pg. 3
- Federal officials warn consumers against taking any Tylenol capsule products temporarily. Sec. 2, pg. 2.
- Two suburban firefighters, comparing notes, were the first to link Tylenol to the deaths. Sec. 2, pg. 3.
- Cyanide can kill within minutes. A graphic tells of symptoms of the poisoning. Sec. 2, pg. 2.

The Falsified Medicines Directive

Good Morning.

THE SPOKESMAN-REVIEW

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United Jet Crashes In Colorado, 25 Killed

Sudafed Tampering Discovered

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Drugs

Nurofen Plus warning over mix-up of painkillers and anti-psychotic drugs

Regulators issue alert after strips of Seroquel XL found in three packets of over-the-counter painkillers brand

Randeep Ramesh

Thursday 25 August 2011 20.43 BST

This article is 4 years old

Shares 1

Save for later

Nurofen Plus packets containing strips of anti-psychotic drug Seroquel XL have been found. Photograph: Reckitt Benckiser

The Falsified Medicines Directive

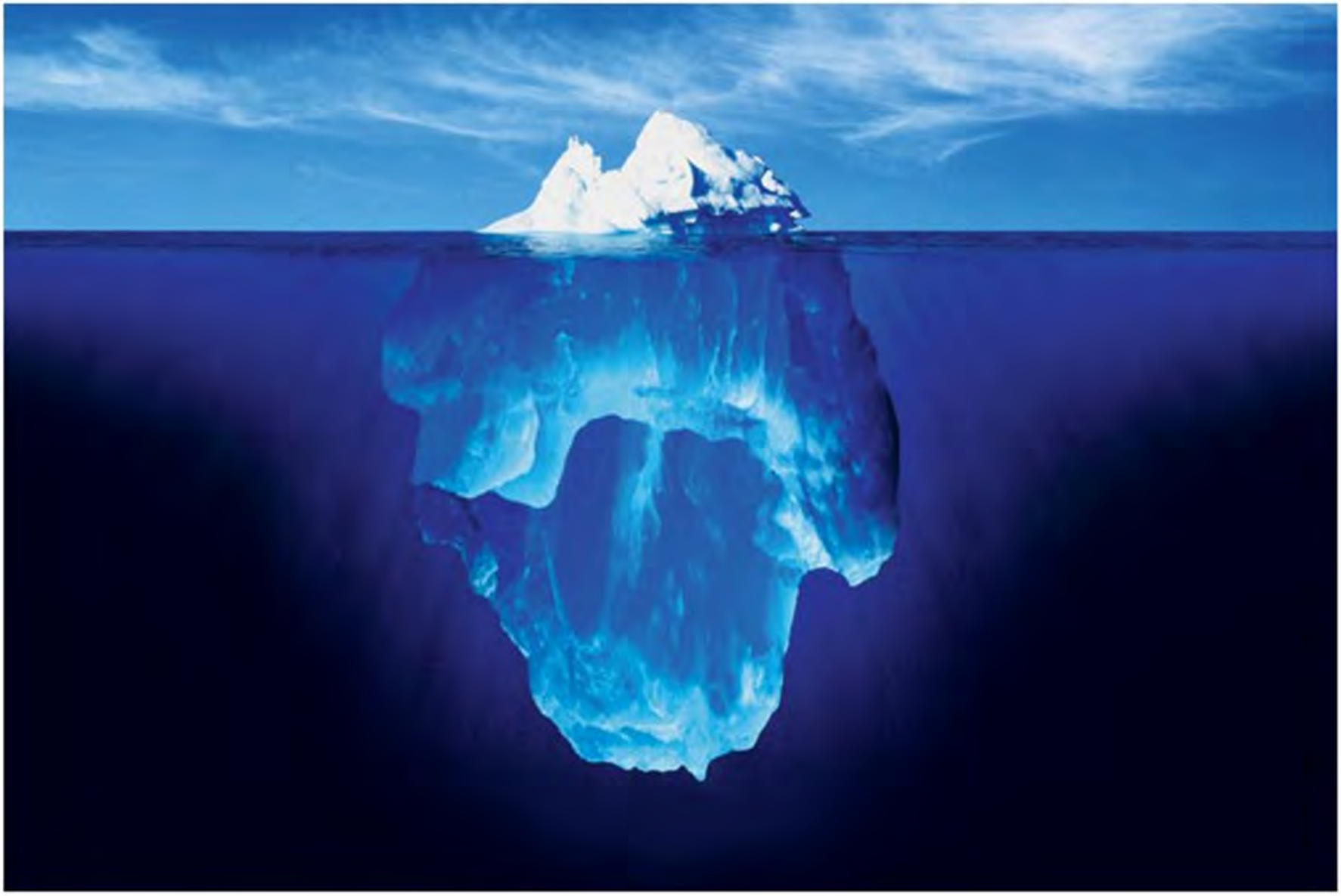
- **Member States may**
  - For the purposes of reimbursement or pharmacovigilance, extend the scope of the application of the unique identifier to any medicinal product subject to prescription or reimbursement
  - For the purposes of patient safety, extend the scope of application of the anti-tampering device to any medicinal product

The Falsified Medicines Directive

- **Member States may**

	Prescription-only	OTC
Unique identifier	Present	Default: No
		MS: Yes (reimbursement or pharmacovigilance)
Anti-tampering device	Present	Default: No
		MS: Yes(patient safety)
28 Member States; product may have different legal status in different MS		

So what should you do?



So what should you do?

- Start preparing! Any manufacturer who has not commenced preparations stands a high probability of not making the deadline.

- Get involved; participate in the consultation! "*Wholesalers and persons authorised or entitled to supply medicinal products to the public are entitled to participate in the legal entity or entities referred to in paragraph 1, on a voluntary basis, at no cost.*"