FALSIFIED MEDICINES: VERIFY BEFORE YOU BUY

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Abstract

Falsified medicines are a global public health risk. This review analyses the evolution of European legislation on counterfeit medicines, requiring individual identification of the packaging of all prescription drugs sold on the Spanish market. The detection of illicit products, safety devices, influencing factors, regularization, control, and the consequences of these, advice for patients, and the incidence rate are some of the topics discussed in depth throughout the paper. In conclusion, the main purpose of future legislation is to ensure consumer safety and harmonization within the EU.

Keywords: unique identifier, anti-tampering device, global trade item number.

Resumen

Los medicamentos falsificados representan un riesgo para la salud pública mundial. En esta revisión se analiza la evolución de la legislación europea en torno a los medicamentos falsificados, que obliga a la identificación individual de los envases de todos los medicamentos de prescripción vendidos en el mercado español. La detección de productos ilícitos, dispositivos de seguridad, factores que influyen en la falsificación, la regularización, control y sus consecuencias, consejos para el paciente y el índice de incidencia son algunos de los temas tratados en profundidad a lo largo del trabajo. En conclusión, la finalidad principal de la futura legislación es garantizar la seguridad del consumidor y la armonización dentro de la Unión Europea.

Palabras clave: identificador único, dispositivos antimanipulación, número comercial global de artículo.

Resum

Els medicaments falsificats representen un risc per a la salut pública mundial. En aquesta revisió, s'analitza l'evolució de la legislació europea entorn dels medicaments falsificats, obligant a la identificació individual dels envasos de tots els medicaments de prescripció venuts en el mercat espanyol. La detecció de productes il·lícits, els dispositius de seguretat, els factors que influeixen en la falsificació, la regularització, el control i les seves conseqüències, els consells per al pacient i l'índex d'incidència són alguns dels temes tractats en profunditat al llarg del treball. En conclusió, la finalitat principal de la futura legislació és garantir la seguretat del consumidor i l'harmonització dins de la UE.

Paraules clau: Identificador únic, dispositius antimanipulació, número comercial global d'article.

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1. Introduction

A falsified medicine is a product deliberately and fraudulently mislabelled as to its identity or source. Falsification affects both branded and generic products. Falsified medicines can range from: accurate products but fake packaging, products with inaccurate or inactive ingredients, or indeed products lacking in active ingredients. Some contain a declared, active ingredient and look so similar to the genuine product that they deceive health professionals as well as patients. But in every case, the source of counterfeit medicine is unknown and its content unreliable (EAASM, 2017, p. 1).

Concern over the quality of medicine is as old as the drugs themselves. It was first approached at the international level in 1985 at the Conference on Rational Use of Medicines in Nairobi. The meeting result was that WHO, together with other international and non-governmental organizations, should consider establishing a focal point to collect data and inform governments about the nature and extent of falsification (WHO, 2017, p. 1).

Due to the World Health Assembly, law enforcement activities were intensified in 2006 and IMPACT was founded, which is composed of international organizations, law enforcement agencies, the pharmaceutical industry and non-governmental organizations. However, the subject did not reach an international level until 2013 at the MEDICRIME Convention, held in Madrid. From that convention, the legal framework for national and international cooperation between health authorities, the police, and customs officials in the fight against falsified products, including medicines, was introduced. After that a total of 23 countries, including Spain, adhered to this initiative (AEMPS, 2016, p. 6-13).

2. Methodology

The essay methodology consists of exhaustive bibliographical research, including a full revision of the _Delegated Regulation (EU) 2016/161_ and reports from government agencies, media reports (non-scientific sources), corporate websites, press releases, and information from non-governmental organizations, supply chain companies and regulatory agencies. The material is based on a search of online databases, including EUR-Lex-UE, using the keywords "counterfeit drugs", "adulterated drugs", "false drugs", and pharmaceutical web companies to obtain graphs.

To carry out the practical part of the work, attendance of the INFARMA congress was useful for contacting several SEVEM managers. Mónica Soler, the Health Sector Manager from AECOC GS1 Spain, was also interviewed, to get her point of view on the verification system. She was of great help, speaking about the development and validation of alternative methods of verifying original medicine.

3. Results

3.1. Legal framework

The current situation follows **Directive 2011/62/EU**, amending **Directive 2001/83/EC** to establish a **community code related to medicinal products for human use, as regards the prevention of the entry into the legal supply chain of falsified medicinal products**. This directive lays down the rules for, inter alia, manufacturing, importing, placing on the
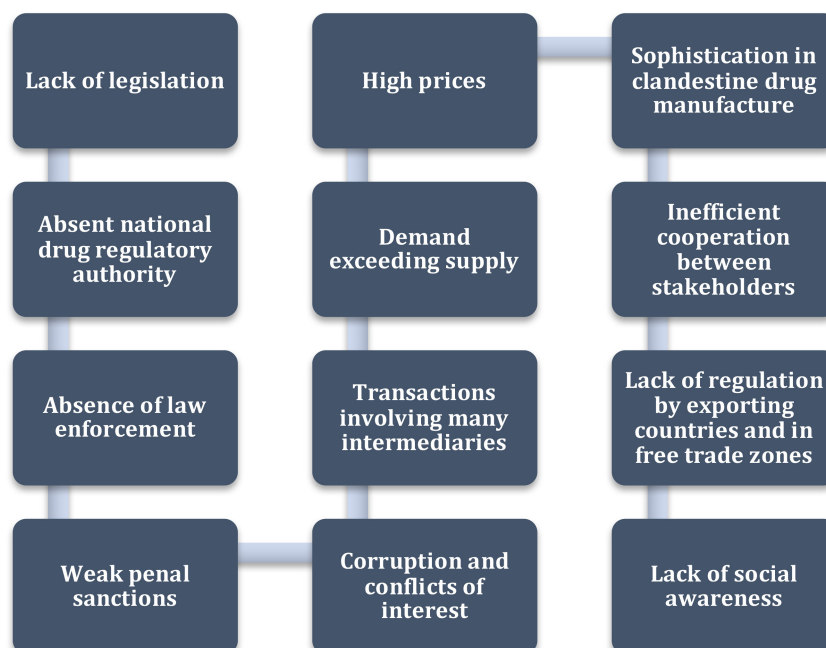
Lack of legislation	High prices	Sophistication in clandestine drug manufacture
Absent national drug regulatory authority	Demand exceeding supply	Inefficient cooperation between stakeholders
Absence of law enforcement	Transactions involving many intermediaries	Lack of regulation by exporting countries and in free trade zones
Weak penal sanctions	Corruption and conflicts of interest	Lack of social awareness

**Figure 1.** General outline of factors facilitating falsifying.

market, and wholesale distribution of medicinal products in the European Union (EU), as well as rules relating to active substances. Past experience shows that such falsified medicinal products can reach patients via both illegal and legal supply chains. This poses a concerning threat to human health. That is the reason why the Directive, which is used at a macro level, should be amended in order to respond to this increasing threat. It also entails international audits, reviews, inspections, sanctions of all forwarding agents, drug control over the internet, and the basic elements for the development of a European model placing <u>safety features</u>, which will allow verification of the authenticity and identification of individual packs and provide evidence of tampering (European Commission, 2017). These safety features for medicinal products should be harmonized within the EU in order to take account of new risk profiles, while ensuring the functioning of the internal market for medicinal products (Soler, M., 2017).

Thus, the system has been developed from the existence of the **Commission *Delegated Regulation (EU) 2016/161* of 2 October 2015 supplementing Directive 2001/83/EC of the European Parliament and of the Council laying down detailed provisions concerning safety devices which are listed on the packaging of medicinal products for human use**, published in the Official Journal on 9 February 2016 (Official Journal of the EU, 2016, L32/1, p. 7-14). The Delegated Regulation describes what new tools will provide detection and prevention of fake drugs entering into the legal supply chain. Its implementation will require all agents in the supply chain as well as the competent authorities. The preparation to carry out these new control mechanisms will be performed during the period of validity of the present strategy, for which reason different actions related to the safety features have been included, such as the <u>unique identifier and the anti-tampering device</u> to ensure the safety of medicinal products. Other measures include: mandatory safety features on the outer packaging of medicines; a common EU-wide logo for identifying legal online pharmacies; tighter standards on controls and inspections of manufacturers of active pharmaceutical ingredients, and, last but not least, strengthening require-

ments for wholesale distributors (Valverde J. L., 2017, p. 1-16). However, this regulation does not mandate the technical options for the anti-tampering device, for which choice of the most appropriate device is left to the manufacturer.

3.2. Drug checking and safety devices system

The Falsified Medicines Directive is being implemented through a European System for the Verification of Medications (EMVS), managed by an international non-profit organization called EMVO, based on serialization packaging through Data Matrix code, to be verified at the point of dispensing (AEMPS, 2016, p. 6-11).
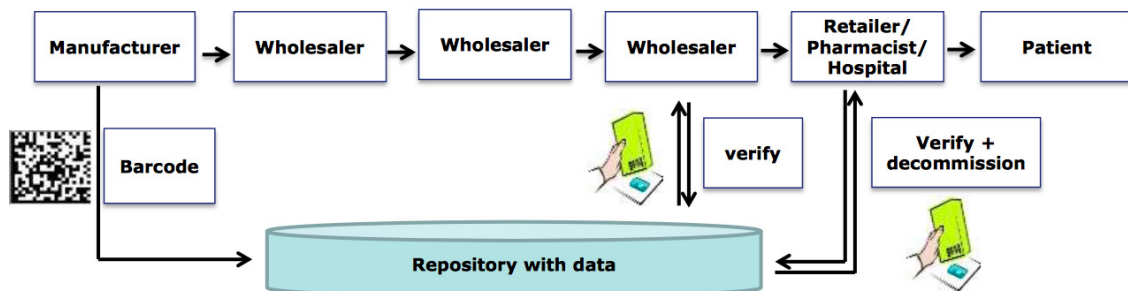
Figure 2. End-to-end verification system + risk based verifications.

What is pursued with the drug verification system is to prevent tampered drugs in the legal supply chain, with each drug packaging being distinctive and increasing controls. In this way, it can be verified that we deal with an original container. The organ in charge of developing, executing and managing the system of verification of medicines is SEVEM.

SEVEM will incorporate a UI to some medicines, which will be recorded in a single database, the repositories system for which will be directly connected to the European
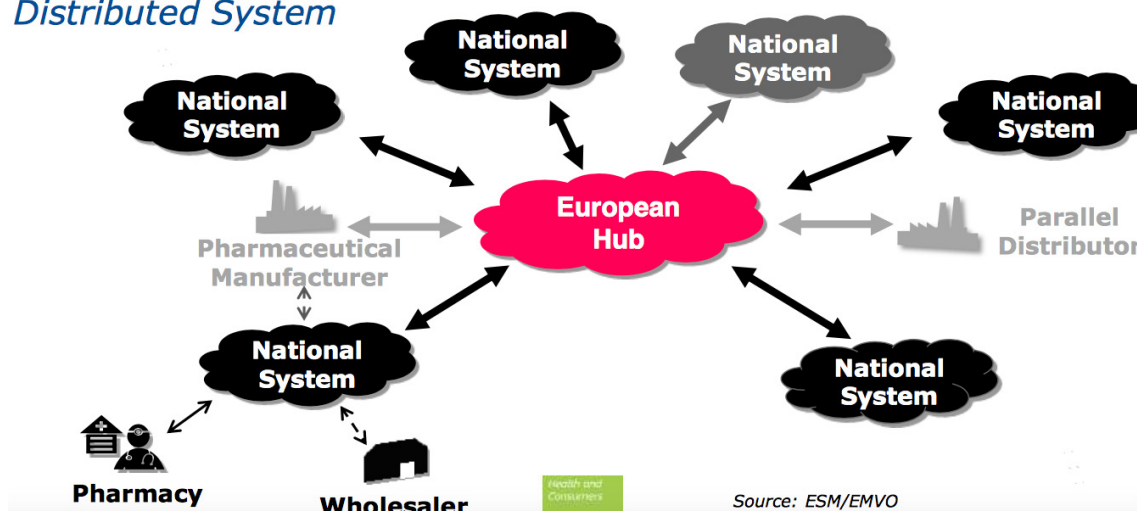
Figure 3. Repositories system architecture.

Hub, a data router. Its main task is to store information on the legitimate UIs and allow its verification/decommissioning at any point of the supply chain. The EU repository will be established and managed by stakeholders. It consists of a central core that will completely connect all national and supranational repositories where all data are identified. The EMVO will manage the European Hub. **The information will reside at the European Hub; however, the verification will be done in the national repository.** The national EMVO is SEVEM. Moreover, the role played by the AEMPS is to enter and monitor, but it is not part of the society that constitutes the SEVEM nor the EMVO (INFARMA, 2017).

3.2.1. Safety devices in the European Union

Directive 2001/62/EC lays down the <u>safety device types</u> and their function, which consist of two elements placed on the packaging of a medicinal product:

1. Verification of the authenticity of individual packs of a drug and its identification through a unique sequence included in a two-dimensional bar code, called a **unique identifier (UI).**
2. A device allowing the verification of whether the packaging of the medicinal product has been tampered with, called an **anti-tampering device (ATD).**

Authorized medicines in Spain that carry the safety devices are all drugs subject to prescription, except those listed in annex 1, the so-called **white list.** Equally, this applies to the non-prescription medicines that must carry them, listed in annex 2, the so-called **black list**. Remarkably, each country will have its own list, and each Member State will extend the scope of the application deciding what drugs will wear the UI and/or the ATD according to *Directive 2001/83/EC.*

Delegated Regulation (EU) 2016/161, applicable from 9 February 2019, contains the characteristics of the UI**,** which is a numerical sequence**,** exclusive for each package, which will consist of (Official Journal of the EU, 2016, L32/1, p. 7-14):

- 14-digit **Product code (GTIN)** that identifies the name, common name, dosage form, dose, size and type of container. In Spain, the Directive leaves several options open for the product code, for example, how will the GTIN be. The GTIN serves for reimbursement and for identification. It has less than 50 characters and is globally unique, issued by ISO-compliant coding agencies.
- Unique **Randomized serial number**, a numeric or alphanumeric sequence of 20 characters maximum, generated by a randomized algorithm, deterministic or non-deterministic.
- **Expiry date** of up to 6 digits (YYMMDD).
- **Batch number** of up to 20 alpha-numeric characters.
- **National reimbursement number or identification number**, if requested by the state where they go to market.

Apart from the UI, a Data Matrix Code, developed in the line with ISO standards, will be added. The two-dimensional barcode can store additional information to the UI data elements. It is robust, with redundant information, so if it is damaged up to 80% it could still be read. This residual storage capacity will be used to include more information without including other barcodes. Also, it is necessary to ensure print quality of the

UI also ISO-compliant (ISO 15418; ISO 15434).

Product code	Serial number	Batch number	Expiry date

(01)09876543210982(21)12345AZRQF1234567890(10)A1C2E3G4I5(17)180531

Illustrative example – not binding

Figure 4. UI model.

two-dimensional barcode structure in order to minimize errors and efficiency reading to facilitate the verification/deactivation of the UI and the act of dispensing (Official Journal of the EU, 2016, L32/1, p. 7-14).

PC: 09876543210982
SN: 12345AZRQF1234567890
NN: (optional)
Batch: A1C2E3G4I5
Expiry: 180531

Illustrative example – not binding

Figure 5. Data Matrix model.

3.2.2. Where should the Unique Identifier be incorporated

Manufacturers will print the barcode on the packaging of all drugs subject to prescription on a smooth, uniform and very reflective surface which at the same time will identify individually each of these to ensure patients' safety. The identification and verification of packaging involves the creation, management of and access to the repositories system, a central data router (hub), and a national or supranational repository connected to the hub, which will store the information on the identification of the packaging unit.

We must be able to identify and verify the authenticity of each drug package all the time that it is on the market, plus the additional time required for the return and disposal of the packaging after its expiry date. The sequence resulting from the combination of the product code and the serial number must be unique for each unit until at least one year after the drug has been released or distributed. Therefore, this will be generated according to specific rules of randomization. The UI must be encoded using a standard syntax and structure data so that it can be decoded and recognized throughout the whole EU through a common scanner (Official Journal of the EU, 2016, L32/1, p. 7-14).

All storing codes will be connected to Nodofarma and the system of repositories at the same time. Nodofarma is a database system that contributes to the digital transformation of the sector. It contains a private cloud dedicated to pharmaceutical services, with high levels of security, confidentiality, availability and integ-

Figure 6. Simulation of container with Data Matrix for unit verification.

rity of transaction data, as well as audit trails throughout the chain (INFARMA, 2017). Moreover, manufacturers must keep transaction records on the drug UI after its deactivation in the repositories system for at least one year after its expiry date or until five years after the medicine has been sold or distributed.

One of the issues to be resolved is the information that will appear in the Data Matrix. The aim is to eliminate the print of the national reimbursement number and insert it in the Data Matrix code to avoid duplicating it. This scenario divides FarmaIndustria. What is clear is that the information of the national code cannot be lost, due to pharmacovigilance issues and the dependency of computer systems on the national code (Diariofarma, 2016). For this reason, there are two possibilities:

1. To include the national code of each presentation directly in the Data Matrix, which means **increasing its size** because it must have five lines for the industry: expiry date, batch number, randomized serial number, national code, and product code. The drawback is that this would slow down production speed. The national reimbursement number would not be printed on the packaging; it could be put in the national repository with the link: CN-CP (Soler, M., 2017).
2. Since the GTIN has served for the refund and for identification, the **National code could be integrated into the structure of the GTIN**. The national reimbursement number would have 14 positions, the same as the GTIN. Moreover, with the large number of new products coming out, the ranks of the seven positions for the refund of a national medical product would be exhausted, whereas the GTIN is inexhaustible and global, unlike the National number identifying the medical product. This is the most supported solution (Soler, M., 2017).

It will have to appear in human reading format with the GTIN and the serial number on the packaging. Indeed, the disparity of authentication mechanisms limits the circulation of medicines in the EU and inflates costs across the supply chain. Therefore, applicable regulations on security devices are required. Notwithstanding, anti-tampering devices, such as holograms, may be applied on any container as desired, even those not required by law, while the UI is not (Official Journal of the EU, 2016, L32/1, p. 7-14).

3.2.3. Key information for the pharmacist

Decommissioning of the UI in the repositories system must occur at the end of the supply chain, when dispensing the medicine. The pharmacist is responsible for keeping the information updated and ensuring that no medication that is expired, recovered, withdrawn, or reported as stolen reaches the public. Regardless, some packages cannot finally be dispensed. Such is the case, for instance, with drugs that would be distributed outside the EU; those to be destroyed, or those that have been returned and cannot be inventoried.

> **Having completed the decommission of a UI in the repositories system, other packaging bearing the same UI cannot be verified.**

The pharmacist authorized to dispense medication needs to verify the authenticity of the UI compared to the genuine one. An audit trail will be created after the introduction of the UI in the repositories, keeping a complete record of all operations for at least one year after the drug expiry date or five years after it has been put up for sale or distributed. Finally, if everything is correct, the pharmacist will disable it using a common scanner (Escribano, B., 2016, p. 18-22).

On the other hand, if the authenticity of the UI is unconfirmed, a terminal alarm is activated, as a possible incident of forgery, except when the medication appears as recovered or withdrawn for destruction on the screen. The effectiveness of the verification system lies in the subsequent decommissioning of the UI of each package, preventing it from being reused by traffickers (Official Journal of the EU, 2016, L32/1, p. 7-14).

3.2.4. Change of status of a Unique Identifier: disabled/enabled

This action can be performed by manufacturers, wholesalers, and persons authorized to dispense drugs, such as pharmacists. The change is carried out if (Official Journal of the EU, 2016, L32/1, p. 7-14):

1. The person making the change has the same authorization and works in the same facility as the person who cancels the UI.
2. The change takes place no more than ten days after deactivation.
3. The drug has not expired.
4. The packaging does not appear in the system repositories as recovered, withdrawn, for destruction or stolen, or the person making the change becomes aware of the theft.
5. The drug has been dispensed.

3.2.5. Manufacturers, industry wholesalers and community pharmacies

Manufacturers, wholesalers, and dispensing entities will verify the authenticity of the UI, comparing it to the UI in the updated repositories system and the integrity of the ATD. They will be identified as authorized to be connected to the repository.

The first intermediaries are the **manufacturers**, who will perform the verification meeting the UI requirements; the registration of all UI operations; verifications prior to re-labelling; decommissioning of the UI; if necessary, the reactivation of the UI, and a diligence actuation in case of tampering (Escribano, B., 2016, p.18-22). Certainly, including the safety devices (UI and ATD) would require access to the European platform (OBP), which is the resolutions technology supplier that protects the confidentiality of data, and loading codes. They also need to maintain relations with SEVEM and the Operations Committee. Manufacturers need to ensure that payment is made using the system, the so-called implementation and maintenance phase, where they still have to establish the rules (INFARMA, 2017).

Secondly, **wholesalers** will have to face costs to adapt the technology to the new system. The software will need to be adapted to carry out risk-based UI checks, at least on returned drugs (by other wholesalers or by dispensing entities). Some of the wholesalers' responsibilities are to take measures in case of manipulation; the decommissioning of the UI and, if necessary, the reactivation of the same. They should also incorporate code readers. In addition, the system offers improvements in batch management, but does

not signify the disappearance of the coupon seal system, as in Spain this is a billing item and nothing to do with the function of the UI (INFARMA, 2017). Exceptions to the end-to-end system are, for instance, that some Member States can be exempt from having the verification/decommissioning obligations of certain items if they are authorized for public supply in the case of veterinarians, dentists, opticians or paramedics, for example. In this situation, the verification/decommissioning of the UI is performed by the wholesaler supplier. What Member States cannot do is to exempt pharmacies or healthcare institutions (Tosetti, P., 2016, p. 2-23).

Finally, **community pharmacies** will perform the verification of the UI and ATD before dispensing the medications; decommission the UI and, if necessary, perform its reactivation, as well as take measures in case of alleged falsification. The logic of the business for the pharmacy is to have a double dispensation control by default; drug verification entry at the pharmacy; manual verification for reading problems; a continuity plan – storage of deactivations by network or system drop; control screen and verification error messages, and integration of verification as the final step of the dispensing process in the electronic prescription. Furthermore, a major investment in computers, equipment and optical readers should be made (INFARMA, 2017).

However, it should be noted that pharmaceutical products put up for sale or distributed before 9 February 2019, may continue to be marketed until their expiry date (Escribano, B., 2016, p. 18-22).

3.3. Cost and implementation path in Spain

#### 3.3.1. Cost of implementation and financing model in Spain

This section starts with a review of the cost of adapting production lines for unit verification, which will represent € 200 million for the pharmaceutical industry in Spain. This figure is based on an estimation made by FarmaIndustria, taking into account a unit cost that could be between € 200,000 and € 400,000. Moreover, safety devices for each package serialization should be added. The quantity mentioned before is just to adapt the machinery and start work. Subsequently, there will be operating expenses, for instance, the security seals that each container will have to carry. Furthermore, the cost of one production line printing the Data Matrix and serializing every single package amounts to € 300,000. In fact, € 150,000 will be needed for technology to insert the anti-tampering device in every container.

Apart from the costs mentioned above, there are fees that will be based on a calculation quota in order to support SEVEM. According to the estimates made they will amount to € 5 million per year. The pharmaceutical industry will have to assume the costs of the start-up and maintenance of the national system and the European node, which FarmaIndustria estimates is between 10 and 13 million euros for launch between 2016 and 2018, and between 5.5 and 8 million euros for 2019.

Another cost that will affect community pharmacies, hospitals and the wholesale sector is that of the capability to read Data Matrix codes. An investment that will have to be made before 9 February 2019, the date by which a drug can only be dispensed in the EU if its authenticity has been verified. Of course, community pharmacies will have a certain settling time and will be allowed to sell all medicines that have no safety devices (Arganda, C., 2016).

3.3.2. Implementation schedule and route sheet

The roadmap for the implementation is organized in four phases:
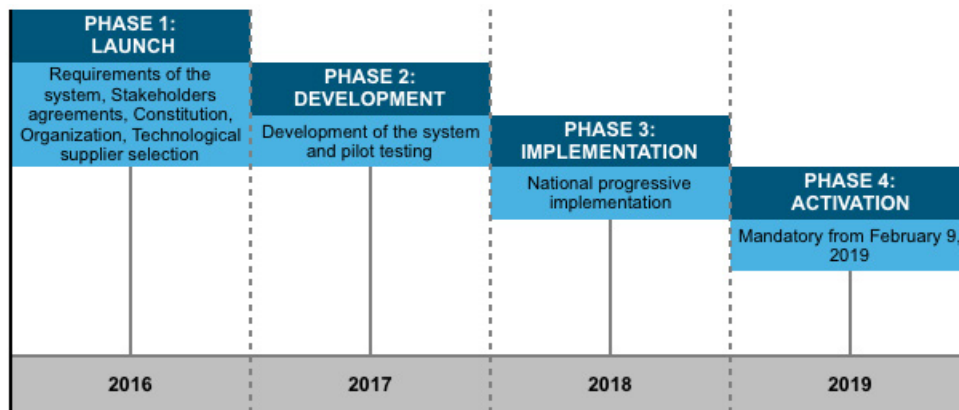
Figure 7. Implementation schedule of the verification system.

Implementation of the new security system was been planned for SEVEM in four phases. The first was the launch: by the end of June 2016, the company had been formed by different agents and, before the year's end, contracts were awarded to the technology provider. In 2017, the development phase, pilot testing took place. In 2018, the third phase will lead to the project's gradual implementation in all pharmacies and hospital pharmacy services. The fourth phase, activation, will begin in February 2019, with the coexistence of prescription drugs with and without safety devices until the year 2024, when all prescription drugs will have to be incorporated into the new model (Granjo, M., 2016).

Regarding the repository system, the development of the European node (EMVO) was completed in 2015. First connection to the national node Securpharm was established in July of that same year. It is a large, complex system that connects to 150,000 pharmacies, 10,000 wholesalers, hospitals, and other dispensing points in Europe. In Spain, the repository development phase is being carried out. The pilot phase was expected to start with wholesalers and pharmacies during the month of July 2017.

Current programme progress includes: 16 NMVOs (50%) founded and four contracts signed; the vast majority of countries aimed for provider contracts in 2017. To sum up: two thirds of all countries are still behind schedule, four countries have not even started the technical work stream, and stakeholder alignment is not completed in some countries, meaning that pharmacies and wholesalers have not been integrated in the NMVO set-up (Walter, A. M., 2017, p.31-2). It can be seen in the figure below that Spain is in the main stream, whereas Germany, Sweden and Finland are perfectly prepared for the real change.
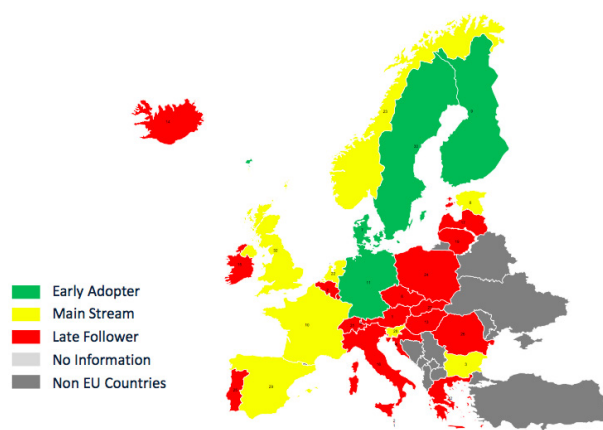
Figure 8. Executive Summary Country Readiness.

68

3.4. The magnitude of the problem

In recent years, there has been a significant increase in the purchase of falsified medicines through non-official channels, like the internet. It was estimated that in 2010 the sale of fake medicines reached $**75,000 million**. Seizures of drugs at the borders of the EU have also proliferated, from half a million containers in 2005 to more than four million in 2007, which means that it has multiplied by seven in just two years (Pfizer, 2015, p. 6-9).

Number of containers seized at European borders

2005: 560.593
2007: 4.081.056
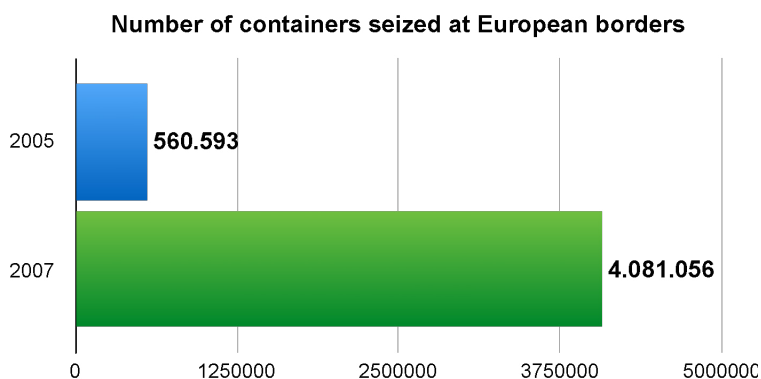
Graphic 1. Number of containers seized in Europe.

To give an **international overview**, studies conducted by the WHO reveal that one out of every ten drugs sold in the world are false; a ratio that corresponds to 50% in developing countries. Most industrialized countries with effective regulatory systems and market controls (e.g. USA, EU, Australia, Canada, Japan, New Zealand) currently have a very low proportion, at less than 1% of the market value. However, developing continents such as Africa, Asia and Latin America have areas where more than 30% of medicines sold are adulterated (FIP, 2016, 32 p. 9-21). In addition, PSI has documented 3,002 incidents of pharmaceutical crime during the calendar year of 2015. In conclusion, from 2011 to 2015 the total number of incidents has increased by 51% (PSI, 2015)
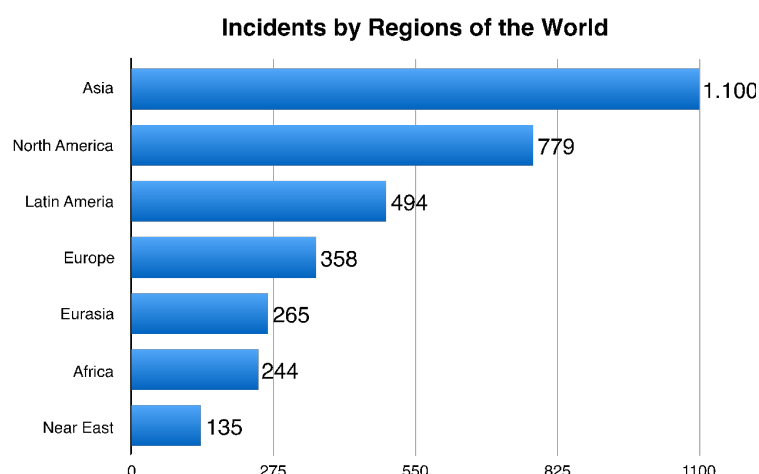
> **At least 50% of medicines purchased online come from an undisclosed physical address and are unreliable.**

3.4.1. Geographic distribution

No continents remain untouched by this issue. With the exponential expansion of internet connectivity, those engaged in the manufacture, distribution and supply of illegitimate products have gained access to a global marketplace. However, it is low- and middle-income countries and areas of conflict or civil unrest that bear the greatest burden of spurious products (WHO, 2017).

As a point of interest, the graphic below shows the geographic distribution of fraudulence, where data is divided into seven regions worldwide, listed from the highest number of incidents to the lowest. A total of 3,002 episodes were recorded and it is concluded that 128 countries are affected by this type of drug crime. It should be emphasized that compared to 2014, PSI recorded a 38% growth in global incidents, and in 2015 the

impact on the Asian region surpassed 1,000 cases for the first time. The same occurred in North America, which saw a 100% increase compared to 2014 (PSI, 2015).

Incidents by Regions of the World

Region	Incidents
Asia	1.100
North America	779
Latin Ameria	494
Europe	358
Eurasia	265
Africa	244
Near East	135

Graphic 2. Incidents recorded per world region in 2015.

3.4.2. Economic impact

The imitation of medicines is very lucrative, worth around $75,000 million. Falsifiers do not spend money on good manufacturing practices, but invest in packaging equipment. It is hard to believe that profit margins can be 500 times higher than the initial cost (Walter, A. M., 2017, 52 p. 31-2)

To make matters worse, the loss of profits due to falsified drug sales is estimated to be $75 billion. To illustrate the point, assuming that only 50% of drug sales would occur at customary prices and that spurious products are most prevalent among the more profitable drugs, the annual commercial profits lost could be approximately $18 billion.
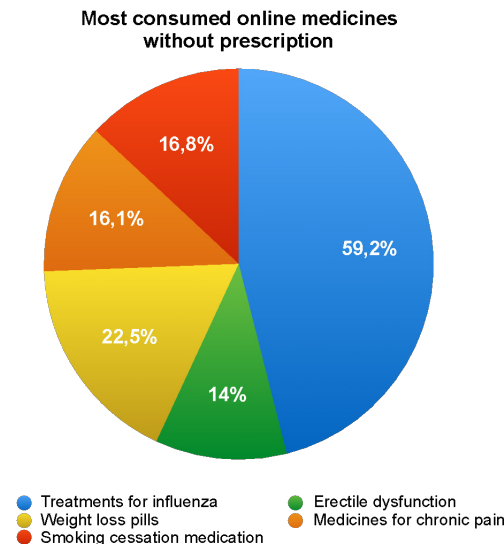
3.5. Analysis of the dilemma

The **"Cracking Counterfeit Europe"** study, conducted by Pfizer in November 2009, sought to assess the real size of the illegal drug market in Europe through an online survey on fake medicines. Some 14,000 people in 14 European countries were surveyed to analyze consumer attitudes about the risks of acquiring prescription drugs through illicit channels. Moreover, to make consumers aware of their treatments under medical prescription always within the legitimate health systems (Pfizer, 2015, p. 6-9).

> **The illegitimate Spanish market could exceed € 1.5 billion annually; 14.3% of the total European black market is estimated to be € 10.5 billion.**
>
> **Almost one in three Spanish people (29.8%) surveyed – approximately 11 million people – admits to having acquired prescription drugs through unofficial sources.**
>
> **The European average of people who buy prescription drugs through illicit channels is 21%, which places Spain in fourth position, behind Germany (38%), Italy (37%) and Norway (30%).**

The most consumed medicines purchased online without a prescription when needed are:[2]

Most consumed online medicines without prescription

- ● Treatments for influenza
- ● Weight loss pills
- ● Smoking cessation medication
- ● Erectile dysfunction
- ● Medicines for chronic pain

Graphic 3. Most consumed online medicines.

Among people in Spain who admitted buying prescription drugs through illicit channels, almost one in five (18%) did so through the internet. Of these, more than a third of purchases were made through foreign pages, and 20% were made after receiving advertising on these medicines through spam mail. According to the study, among the ones who admitted having acquired fraudulent drugs, 24% of the respondents detected that the medicine was false, 40% considered that the medicine did not work, and 37% said that it was not safe. The main reason people get prescription drugs on the internet is to save time and money, with the cost issue being more important than time.

According to the results of the study, one out of every five Spanish respondents, extrapolated to a percentage of the total Spanish population (representing more than 7.5 million people) do not consider that the consumption of drugs without prescription is a risk to their health. More than two-thirds of the Spanish population (67%) would not buy medicine over the internet if they knew it was false. However, a worrying 13% of respondents in Spain consider that the chance of getting a fake product would not impact on their intention to make such a purchase (Pfizer, 2015, p. 6-9).

4. Conclusions

Falsified medicines are a major problem worldwide, affecting all countries in different ways. Unfortunately, it is not sufficient to only solve the problem of the illegal transit of modified drugs, but it is also important to ensure that patients do not lose faith in the benefits of medicines and following proper treatment. The growth of the internet and the increasing difficulty of monitoring suppliers has led to an exponentially higher pro-

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[2] It should be noted that the survey was conducted in November 2009, in the midst of the media boom of influenza A.

portion of consumers purchasing non-genuine drugs. Evidently, national and international harmonization to identify falsified medicines is needed, and this requires excellent coordination to ensure good success in the search of imitations.

It is quite complex to measure the actual extent of the drug adulteration dilemma and its real impact, especially in developing countries where the percentage of replica products is higher. This issue goes hand in hand with the increase in intermediaries, non-existent regulations, and price differences in some countries compared to others, due to the lack of adequate reimbursement plans which boost illegal trade. These facts encourage patients to look for cheaper and more accessible alternatives, for instance, on the internet.

It should be noted that the harmful consequences to human health show that the risk is not so hypothetical. It is extremely difficult to detect the cause of a disease if there are doubts about having consumed a manipulated medicine. For this reason, medical doctors have a pivotal role, to curb and prevent the phenomenon, especially among older people, since many of them are polymedicated and may suffer more drug interactions. On the other hand, fraudulent drug consumption also represents greater economic expense for public health due to increased hospital admissions.

In a nutshell, there must be a continuous effort to ensure that adulterated drugs are found, reported, and withdrawn from the market. In this sense, the vital benefits of serialization should be highlighted, beyond fulfilling its essential function. The main advantage associated with this is to provide greater drug security and guarantee laboratory supplies. Similarly, it remains to be determined how the new labelling will influence a reduction of the products withdrawn from the market. In general, the technological processes of validation and control of packaging will improve, and thus errors will be drastically reduced. Other strengths include having greater visibility of products, and improved withdrawal speeds for those already placed on the market. This will be reflected in an upgrade in the control of the expiry date and storage containers. On the other hand, a remarkable point will be the future eradication of the coupon seal , as has happened in France. This will be made possible thanks to the 2D code that will include more information, such as the product code, batch number, expiry date and serial number.

Patient safety is certainly the main benefit, but so is the protection of commercial firms. The advertising associated with any incidence of counterfeiting creates a strong threat, endangering the reputation of even the most powerful brands. So much so, that new guidelines on good distribution practice are far more detailed, with stricter requirements on management of suppliers and customer quality control systems: a helpful fact for the security and transparency of the distribution chain entities. On the economic issue, FarmaIndustria will make a great investment in the expectation that they will later recover the benefits of eliminating fakes. Regrettably the new strategy will be implemented late in Spain due to structural reasons.

Although our society is experiencing a greater awareness of the harmful effects that involve the intake of an imitation drug, there is still much work to do and a greater effort is required in terms of cooperation and collaboration among governments and organizations to be successful. It is a general aim that all pharmacists learn about the existing challenge, as they are the final members of the supply chain. Also, it is vitally important to improve their professional skills in the fight against falsified drugs. Ultimately, this review reflects the social impact of the trouble, and aims to provoke a reaction in the reader of precaution toward everything purchased and awareness of the future changes that will arise from this new regulation, making Spain not only a safer, but also a more modern, efficient and competitive sector.

72

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