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SERIALIZATION – LEGAL AND INFORMATION TECHNOLOGY FRAMEWORK TO TRACK PRODUCT FROM PRODUCER TO CUSTOMER

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ABSTRACT

Quality of product and safety of product usage is of key importance in different industries specifically in health and pharmaceutical industry. Internet becomes a framework for new e-economy development bringing new and inventive opportunities for business development. But in the same time Internet becomes largest channel for selling fake, counterfeit and misbranded products and pharmaceutical products specially, threating people's life and public health. To solve this problem number of countries in the world started implementation of track and trace systems that will enable customer and authorities to track production and logistic chain for specific product from the trader, to the producer and even to the row material producer of product. This is not a simple task, since it requires adequate legal framework and information technology system development. The purpose of this paper is to explain legal framework and information technology terms and procedures related with serialization. A brief overview of serialization implementation in different countries and EU is given. Legal and IT framework is presented for EU. Product counterfeiting is a general problem which importance grows in e-commerce environment. Thus serialization in pharmaceutical industries is just beginning; it will be base for future development and spreading this solution in other industries as well.

1. INTRODUCTION

The application of different information technologies (IT) makes our world functioning. IT technologies applications optimize business processes within or between different organizations, and today there is not even single aspect of business process in which IT does not take important role. The product which we are purchasing and using has to fulfill our needs and wishes. Product

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characteristics must be declared, since it is base for searching and selecting them on Internet. In Internet and e-commerce environment customer has no physical contact with product. Thus description, photo, video or virtual reality presentation and of course, the brand are source of information and selection for customer. Product information is mainly generated by the trader or producer, but some of the additional information can be generated by product user, their product ratings, experiences and opinions are published on the product web page, distributed thru different social services and social networks.

Nevertheless in product selection process one of the strongest influences beside the price, has the product brand as well. We are usually more attracted by the product with better brand image. It is no wonder since the brand is tightly connected with company reputation and quality of the product. But large proportion of products on the market, in the stores, on Internet is fake products. Fake medicine or food can be dangerous or even lethal. Product serialization shall ensure customer that the product which he or she are paying is original, not fake, and not counterfeit and that this product has required and declared characteristics. Serialization is base for any track and trace system, "it is assignment a unique traceable number to each saleable package unit of product"[1]. A serial number must be assigned to each container as product moves thru different package phases. Every blister, bottle, box or pallet must be uniquely identified with serial number.

2. SERIALIZATION IMPLEMENTATION BRIEF OVERVIEW

One of the key events in serialization introduction into practice was Prescription Drug Marketing Act (PDMA) in USA from 1987. "The PDMA was enacted (1) to ensure that drug products purchased by consumers are safe and effective, and (2) to avoid the unacceptable risk to American consumers from counterfeit, adulterated, misbranded, sub potent, or expired drugs. The legislation was necessary to increase safeguards in the drug distribution system to prevent the introduction and retail sale of substandard, ineffective, or counterfeit drugs"[2]. Soon special Counterfeit Drug Task Force was established in 2003 by FDA to enhance the existing safeguards that are in place to protect the nation's drug supply from counterfeit drugs.[3].

[1] Buker Dana, Loy David: Serialization – A Worldwide Challenge, Pharmaceutical Engineering, September/October 2012, Vol. 32 No.5. page 1. http://www.ispe.org/pharmaceutical_engineering/12so-buker.pdf (05.2016)

[2] http://www.fda.gov/RegulatoryInformation/Legislation/SignificantAmendmentstotheFDCAct/PrescriptionDrugMarketingActof1987/default.htm (05.2016)

[3] http://www.fda.gov/Drugs/DrugSafety/ucm174399.htm (05.2016)

In 2003 Belgium published a Royal Decree[4] introducing obligation of sequential codes application on all medicine products to identify uniquely every product pack. All packages from 2004 must have 16-digit bar code product identification number. In USA 2004 California Ridley-Thomas Pharmacy Pedigree SB 1307 establish base to provide "means an electronic record containing information regarding each transaction resulting in a change of ownership of a given dangerous drug, from sale by a manufacturer, through acquisition and sale by one or more wholesalers, manufacturers, or pharmacies, until final sale to a pharmacy or other person furnishing, administering, or dispensing the dangerous drug"[5].

In 2008 China Chinese State Food and Drug Administration (CFDA) made serialization mandatory on individual saleable pharmaceutical product units for 275 therapeutic classes by December 2011. [6]

Brazil in 2009 established rules and provisions for implementation of a national system of drug product identification and tracking throughout the pharmaceutical supply chain, Resolution No. 54, by the Joint Board of the National Health Surveillance Agency (ANVISA – Agencia Nacional de Vigilancia Sanitariar)[7].

In France from January, 2011 CIP13 coding legislation defined by Agency of Sanitary Safety and Health Products (AFSSAPS) requires all prescribed pharmaceutical products to include a specified data matrix barcode on the outer packaging. Manufacturers, distributors, pharmacies and hospitals must trace products by electronic receipt notice[8].

South Korean Ministry of Health and Welfare notification 2011- 58, amending "Controlling and indicating barcodes of pharmaceutical products," establishes new regulations relating to drug traceability. In Turkey in 2012, the Turkish Ministry of Health (MOH) established the ITS system (Ilaç Takip Sistemi, or

4 https://www.cov.com/-/media/files/corporate/publications/2003/03/oid6036.pdf

5 http://leginfo.legislature.ca.gov/faces/billNavClient.xhtml?bill_id=200720080SB1307 (05.2016)

6 According to: Pharmaceutical Track-And-Trace Serialization Playbook, 2016 Edition, Health Care Packaging, http://www.healthcarepackaging.com/playbooks/pharmaceutical-serialization-playbook (05.2016)

7 According to: Pharmaceutical Serialization Track And Trace (Easy guide to country-wise mandates), page 4 https://www.infosys.com/industries/life-sciences/industry-offerings/Documents/pharmaceutical-serialization-country-wise-mandates.pdf (05.2016)

8 According to: Pharmaceutical Serialization Track And Trace (Easy guide to country-wise mandates), page 4 https://www.infosys.com/industries/life-sciences/industry-offerings/Documents/pharmaceutical-serialization-country-wise-mandates.pdf (05.2016) p.4.

Pharmaceutical Track and Trace System) to track prescription drug products and their shipping cases.

Argentine law requires serializing and tracking using GS1 encoded DataMatrix symbols for all unit-level items that are reimbursed. The National Food, Drug and Technology Administration (ANMAT), has chosen GS1 Standards to identify drugs through the supply chain[9].

In India, serialization begins in 2015. The Indian Directorate General of Foreign Trade (DGFT) requires GS1-GTIN, serialization and barcodes on tertiary (cases), secondary and primary packaging for all pharmaceuticals exported from the country[10].

In Saudi Arabia, serialization is obligatory after March 23, 2015, and in Jordan after January 1, 2017. In both countries the outer package of prescription drug products must contain both a human readable, and a DataMatrix, symbol encoded with GS1-GTIN to identify the item, the packaging lot number, expiration date and pack size. [11]

3. EU REGULATORY FRAMEWORK

"The high level of human health protection should be ensured in the definition and implementation of all EU policies and activities"[12]. In achieving this goal producers and distributers should complain to required and expected production and distribution standards for different products.

Falsified medicines are a major threat to public health and safety, since they have not been properly evaluated to check their quality, safety and efficacy - as required by strict EU authorization procedures[13]. It might contain ingredients of bad quality or in the wrong dose. As falsifications become more sophisti-

[9] According to: Pharmaceutical Track-And-Trace Serialization Playbook, 2016 Edition, Health Care Packaging, http://www.healthcarepackaging.com/playbooks/pharmaceutical-serialization-playbook (05.2016)

[10] According to: Pharmaceutical Track-And-Trace Serialization Playbook, 2016 Edition, Health Care Packaging, http://www.healthcarepackaging.com/playbooks/pharmaceutical-serialization-playbook (05.2016)

[11] Data according to: Pharmaceutical Track-And-Trace Serialization Playbook, 2016 Edition, Health Care Packaging, p.25-26. http://www.healthcarepackaging.com/playbooks/pharmaceutical-serialization-playbook (05.2016)

[12] TFEU article 168 https://europadatenbank.iaaeu.de/user/view_legalact.php?id=260 (05.2016)

[13] According to: European Medicine Agency: Falsified medicine, http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000186.jsp (05.2016)

cated, the risk that falsified or counterfeit medicines enter in the EU market increases every year. In period 1988-2004 increase in counterfeit seizures was 1000 %[14]. Falsified medicines represent a serious threat to global health and call for a comprehensive strategy both at European and international level[15].

National health measures fall within internal market rules, and medical goods and services doesn't have any special status, and the free movement must be guaranteed to the same subject as any other goods or services.

Most falsified medicine in developed countries is lifestyle expensive products hormone, steroids, antihistaminic, corticosteroids, obesity and erectile dysfunction. In developing countries most of falsified medicine is one for life threatening diseases oncological, antibiotics, cardiovascular, pain killers.[16]. Fake medicine distribution channels are door to door sale, or legal chain of distribution through wholesalers (cca.2%). But the largest channel for fake medicine distribution is Internet, over 50%.[17]

The EU has a strong legal framework for the licensing, manufacturing and distribution of medicines. At the end of the distribution chain, only licensed pharmacies and approved retailers are allowed to offer medicines for sale, including the legitimate sale via the Internet.

The "Medicrime Convention" is the first international criminal law instrument to oblige States Parties to criminalize[18] the manufacturing of counterfeit medical products; supplying, offering to supply and trafficking in counterfeit medical products; the falsification of documents; the unauthorized manufacturing or supplying of medicinal products and the placing on the market of medical devices which do not comply with conformity requirements.

The Convention provides a framework for national and international co-operation across the different sectors of the public administration, measures for coordination at national level, preventive measures for use by public and pri-

[14] Atzor Sabine, DG ENTR Study on Distribution Channels: Part I Combating Counterfeit Medicines, Stakeholder Meeting 29 November 2006, http://ec.europa.eu/health/files/counterf_par_trade/2006_11_com_pres_counterfeitstrategy_en.pdf (05.2016)

[15] WHO estimated that counterfeit and fake medicine are responsible for hundreds thousands death in the world Sanofi: The Fight Against Counterfeit Medicines, November, 2015, http://en.sanofi.com/Images/40228_Presskit_2015-12_Counterfeit_EN_V2.pdf (05.2016) p. 3

[16] According to: European Medicine Agency: Falsified medicine, http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000186.jsp (05.2016)

[17] Sanofi: The Fight Against Counterfeit Medicines, November, 2015, http://en.sanofi.com/Images/40228_Presskit_2015-12_Counterfeit_EN_V2.pdf (05.2016) p. 5

[18] CETS 211 – Counterfeiting of medical products and similar crimes, 28.X.2011:http://www.coe.int/en/web/conventions/full-list/-/conventions/rms/090000168008482f (05.2016) p.5

vate sectors and protection of victims and witnesses. Furthermore, it foresees the establishment of a monitoring body to oversee the implementation of the Convention by the States Parties.

In July 2011, the EU strengthened the protection of patients and consumers by adopting a new Directive on falsified medicines for human use[19]. The Falsified Medicines Directive applies since 2 January 2013. The Directive introduces tougher rules to improve the protection of public health with new harmonized, pan-European measures to ensure that medicines are safe and that the trade in medicines is rigorously controlled. These new measures include[20]:

- Obligatory safety features on the outer packaging of the medicines, to be detailed via a delegated act;
- A common, EU-wide logo to identify legal online pharmacies. This would make it easier to distinguish between legal and illegal online pharmacies throughout the European Union;
- Tougher rules on the controls and inspections of producers of active pharmaceutical ingredients;
- Strengthened record-keeping requirements for wholesale distributors

On 9 February 2016, the European Commission published a delegated regulation (Commission Delegated Regulation (EU) 2016/161) that introduces two safety features to be placed on the packaging of most human medicines: a unique identifier (a 2-dimension barcode) and an anti-tampering device[21]. These safety features will guarantee medicine authenticity for the benefit of patients and businesses, and will strengthen the security of the medicine supply chain, from manufacturers to distributors, pharmacies and hospitals. Marketing authorization holders must place these on the packaging of most prescription medicines and certain non-prescription medicines no later than 9 February 2019. The annexes of the regulation include the list of medicines subject to the new requirement[22]. Regulation (EU) 2016/161 mainly provides for: technical characteristics of the unique identifier (UI), verification of the Safety Features, repositories system for the UI, lists of exceptions from bearing/not bearing the safety features. European Medical Association (EMA) and the

[19] EU Directive: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:174:0074:0087:EN:PDF (05.2016)

[20] EU Directive: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri= J:L:2011:174:0074:0087:EN:PDF (05.2016)

[21] Commision Delegated Regulation (EU) 2016/161 of 2 October 2015: http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0161&from=EN (05.2016)

[22] According to: European Medicine Agency: Falsified medicine, http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000186.jsp (05.2016)

European Commission have prepared an implementation plan, including regulatory requirements and timelines, to guide applicants and marketing authorization holders of centrally authorized medicines in meeting the requirements.

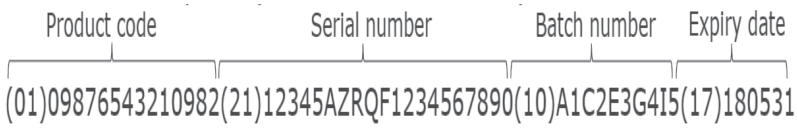
Tamper is packaging that makes tampering apparent to the observer, to some degree. Drugs need more care in their packaging than do most other products, because any failure in their packaging could result in changes in the drug that lead either to a failure to cure to illness to injury or even to death of the patient. Modern packaging needs to be child resistant and tamper evident. Convenience, ease of use, hygiene package integrity and new dispensing methods must now also be provided for patient and is part of safety features[23].

4. PROCEDURE AND IT FRAMEWORK

Outer package of each product unit must contain unique identifier (figure 1). It consists of[24]

- Product code: ISO-compliant (ISO 15459); < 50 characters; globally unique; issued by ISO-compliant coding agencies;
- Serial number (max 20 characters; randomized)
- A national reimbursement or identification number (optional)
- Batch number
- Expiry date

Figure 1. structure of product unique identifier[25]



The UI is carried by a 2D barcode (Data Matrix ECC200) printed on the outer package of the medicine, minimum printing quality and Human-readable format.

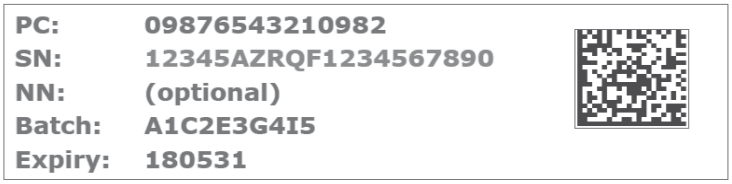
[23] According to: Manoj Shivaji Kumbhar, Naresh Hiraram Choudhary, Deepak Annasaheb Dighe, Meera Chandradatt Singh Sinhgad: Tamper Evident Pharmaceutical Packaging – Needs and Advances, International Journal of Pharmaceutical Sciences Review and Research, P. 141, Available online at www.globalresearchonline.net http://globalresearchonline.net/journalcontents/v13-2/030.pdf (05.2016)

[24] Commision Delegated Regulation (EU) 2016/161 of 2 October 2015: http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0161&from=EN (05.2016)

[25] Commision Delegated Regulation (EU) 2016/161 of 2 October 2015: http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0161&from=EN (05.2016)

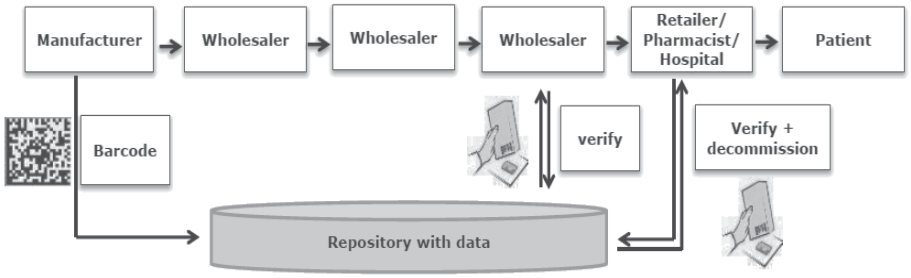
The Data Matrix = only 2D barcode allowed for authentication and identification of a medicinal product. QR codes are allowed, except for identification and authentication. Multiple UIs are allowed, e.g. in case of multi-language packs intended to be marketed in more than one Member State, where each UI contains the specific national reimbursement/ID number of one of the destination Member States.

Figure 2. Product unique identifier - 2 D barcode representation on the product package[26]



At product unique identifier (UI) is printed on the product pack and uploaded in a secure repository system, and ATDs are applied on packs as well. When verifying the authenticity of a unique identifier, manufacturers, wholesalers and persons authorized or entitled to supply medicinal products to the public shall check the unique identifier against the unique identifiers stored in the repositories system (Figure 3. Product verification and decommission). A unique identifier shall be considered authentic when the repositories system contains an active unique identifier with the product code and serial number that are identical to those of the unique identifier being verified. The integrity of the ATD is checked as well.

Figure 3. Distribution, verification and decommission process[27]

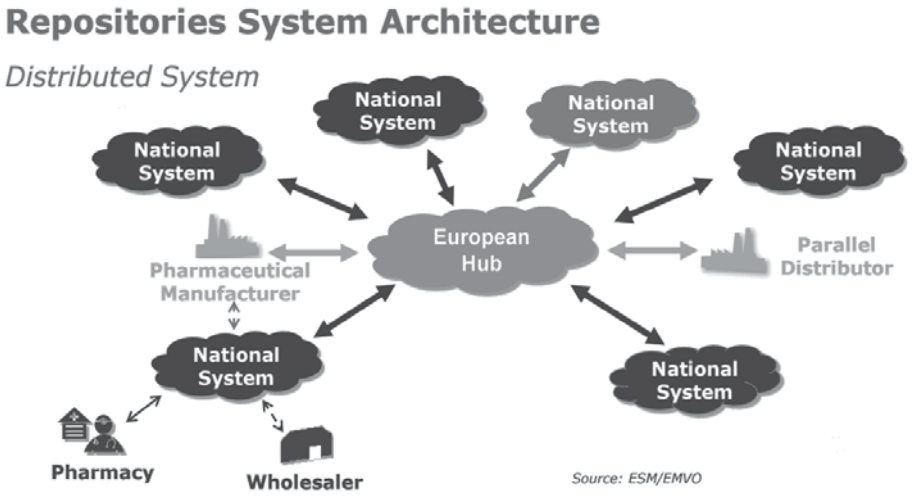


[26] Commision Delegated Regulation (EU) 2016/161 of 2 October 2015: http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0161&from=EN (05.2016)

[27] Tosetti Patrizia: Medicines verification in Europe: What to expect in 2019 Stakeholders' workshop 26 February 2016 DG SANTE, http://ec.europa.eu/health/files/falsified_medicines/201602_stakeholders_workshop_final.pdf (05.2019)

To serialization process must be supported by data repository on national and EU level. It consists of a central information and data router ('hub') and national or supranational repositories connected to the hub (Figure 4). The main task is to store the information of the product unique identifier and allow the verification/decommissioning of them at any point of the supply chain. It is established and managed by stakeholders and supervised by competent authorities.

Figure 4. Repositories system Architecture[28]



The repositories system has to ensure: verification of authenticity and decommissioning of UI, detection of potential incidents of falsification; interoperability among repositories; commercial, confidential and personal data protection; extremely quick response time (300 ms system response time); recording of all operations concerning a UI ('audit trail') [29].

[28] Tosetti Patrizia: Medicines verification in Europe: What to expect in 2019 Stakeholders' workshop 26 February 2016 DG SANTE, http://ec.europa.eu/health/files/falsified_medicines/201602_stakeholders_workshop_final.pdf (05.2019)

[29] Tosetti Patrizia: Medicines verification in Europe: What to expect in 2019 Stakeholders' workshop 26 February 2016 DG SANTE, http://ec.europa.eu/health/files/falsified_medicines/201602_stakeholders_workshop_final.pdf (05.2019)

CONCLUSION

Information and communication technologies (ITC) have enormous potential to improve the quality, safety and efficiency of healthcare. But in the same time as new and innovative space develops a new and innovative way to develop new and innovative way for different illegal activities. ITC solutions become not only tool for achieving regulatory requirements, but become key technology for interconnecting as well as personals, as companies and counties and societies. The number, type, and complexity of different medicaments which are we using are growing very fast. One of the key issues is to prevent distribution and usage of counterfeits and fake and misbranded products threating people's life and public health. Serialization is in different phases of implementation and introduction in number of countries. GS1 Datamatrix[30] is used in all serialization processes except in China.

To accomplish the successful deployment of a global serialization program, flexibility is the key. The system should not be targeted at a single regulation but should be designed to provide building blocks of functionality, which can be applied differently to the same products in different regulatory environments.

The serialization application process started in pharmaceutical and life sciences with necessity to cope with fake, counterfeit and misbranded products and pharmaceutical products specially, threating people's life and public health[31]. Product counterfeiting is a general problem which importance grows in e-commerce environment. Thus serialization in pharmaceutical industries is just beginning; it will be base for future development and spreading this solution in other industries as well.

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