RESEARCH STUDIES

Legal aspects in detecting counterfeit medicines

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Abstract

Background: With the rapid development of the pharmaceutical industry cases of counterfeit medicines are more and more frequent. This is a real crime that influences Public Health, counterfeit medicines being harmful and even fatal.

Material and methods: For this study we carried out an objective analysis of the world legislative framework, with predilection for the European and national one. As landmarks served: setting the research objectives, data collection, data analysis, formulation of results and conclusions.

Results: The number of counterfeiting incidents during 2011 – 2015 constituted: 2011 – 1986 crimes, 2012 – 2018 crimes, 2013 – 2193 crimes, 2014 – 2177 crimes, 2015 – 3002 crimes. So far numerous directives have been approved, laws have been adopted and measures have been taken to stop the counterfeiting of medicines (Directive 2011/62/EU of 8 September 2011, the Convention MEDICRIME, Resolution 65.19 of the World Health Assembly, Rapid Alert System, global and regional operations of Interpol).

Conclusions: Counterfeiting of pharmaceuticals is a global problem that involves: institutions, law enforcement, customs, doctors, pharmacists, patients and citizens. The competent national authorities in collaboration with the associations of doctors, pharmacists and patients must lead risk awareness campaigns regarding purchasing of pharmaceutical products from illegal sources. Patients should be informed of the risks they assume by purchasing drugs from different websites. The population should know that websites that sell drugs must have links directing to the competent national authority or the website of European Medicines Agency or Medicines and Medical Devices Agency from the Republic of Moldova.

Key words: counterfeit medicines, directives, operations, cooperation.

Introduction

With the continuous development of the pharmaceutical industry cases of counterfeit medicines are more and more frequent.

Although the counterfeit medicines manufacture was focused in first place on drugs that don't treat diseases but only improve the quality of life, the manufacturing industry has expanded to cover any type of drugs [1, 2].

Counterfeiting medicines is a real crime, and its severity is not determined only by economic losses which is the main problem for counterfeits in other industries. The drug counterfeit is not only an economic issue but also a Public Health one [3].

Counterfeit medicines are ranked from useless to potentially dangerous. They often contain wrong level of active ingredient – too little, too much or not at all – or an active ingredient intended for a different purpose. In some cases counterfeit drugs containing highly toxic substances such as rat poison were found. In all these scenarios, the person using counterfeit drug puts his health, even his life in danger [4]. Medical products counterfeiting and similar crimes should be classified as criminal actions because of the risk they pose to public health. Disease treatment is delayed due to ineffective counterfeit drugs and illegal products, so the appropriate treatment could be futile because it got too late. Counterfeit medical products and similar crimes are silent killers because the patient could die from illness ineffectively treated. In such cases, no one will look for counterfeiting as a possible cause [2].

WHO estimates that up to 1 percent of medicines available in developed countries are likely to be counterfeited. This figure rises to 10 percent globally, but in some areas of Asia, Africa and Latin America counterfeit medicines are up to 30 percent of the market.

Counterfeiting not only applies to drugs intended for lifestyle, including erectile dysfunction and weight loss, but also vital drugs are more and more often falsified, including those for cancer treatment, cardiac disorders and other severe illness cure [4].

The international and national legal framework shall play the central role in the combat of this inhuman act. So far numerous directives have been approved, laws have been adopted and measures have been taken to stop the counterfeiting of medicines. Are they sufficient?

Global cooperation is the key to efficient fight with counterfeit medicines. A positive aspect in this regard is the involvement and contribution of the Republic of Moldova in this fierce battle against the epidemic of counterfeit medicines.

Material and methods

For this study we carried out an objective analysis of the world legislative framework, with predilection for the European and national one. As landmarks served: setting

the research objectives, data collection, data analysis, formulation of results and conclusions. Data from official sources were studied, such as Quality Control of Medicines Laboratory (QCML), World Health Organization (WHO), Pharmaceutical Security Institute (PSI), European Directorate for the Quality of Medicines (EDQM), INTERPOL, etc. The following methods were used for the analysis: comparative and graphical representation.

Results and discussions

Pharmaceutical legislation was adopted, for the first time 40 years ago and principles of marketing, manufacturing, import, export and distribution as they are today – were adopted in 1975. WHO began fighting counterfeit medicines since the 80s, when manufacturing, distribution and drugs marketing lines were developing. The legislative framework so far has undergone various changes, for better resistance against counterfeiting.

It is very important to make the distinction between substandard and counterfeit drugs. According to WHO a counterfeit medicine is one which is deliberately and fraudulently mislabelled with respect to identity and/or source. Counterfeiting can apply to both branded and generic products and counterfeit products may include products with the correct ingredients or with the wrong ingredients, without active ingredients, with insufficient (inadequate quantities of ingredient(s) or with fake packaging. Substandard medicines (also called out of specification (OOS) products), according to the same source, are genuine medicines produced by manufacturers authorized by the National Medicines Regulatory Authority (NMRA) which do not meet quality specifications set for them by National standards [1].

In this connection we can talk about several types of counterfeiting:

- The drug is perfect imitation of the authentic version. The same active substance and excipients, the correct amounts of API and properly packaged.
- The drug is identical to the authentic version but the amount of active substance differs from that stated on the label and the information related to the source of raw material, validity date, bioavailability doesn't correspond.
- The drug is similar to the authentic version but contains neither active nor harmful substance.
- The medicine appears at first glance similar to the authentic version but does not contain the same active substance and contains harmful substances.
- The drug packaging is fake.

Even if they are of appropriate quality and contain the correct amount of active ingredient, counterfeit medicines do not guarantee quality, as they are not manufactured in accordance with good manufacturing practice (GMP) and good distribution practice (GDP) established globally and imposed by the pharmaceutical industry to products. Counterfeit products do not equivalate their safety, quality and efficacy, characteristic to genuine products [3, 5].

In recent years, according to statistics, we see a continuous growing of crimes in the field of counterfeit drugs, in the chart below are presented the details regarding the number of crimes in pharmaceutical field during the last five years, according to PSI (fig. 1).

To understand better the magnitude of counterfeiting incidents during 2015, PSI continues to monitor the quantity of seized medicines at every action of law enforcement. Any incident, which involves the seizure of more than 1000 dosage units, is classified as commercial incident. The incident involving less than 1000 dosage units is classified as non-commercial one (fig. 2).

All continents and countries are involved in medicines counterfeiting, either directly through the manufacturing, marketing, distribution of counterfeit medicines, or indi-

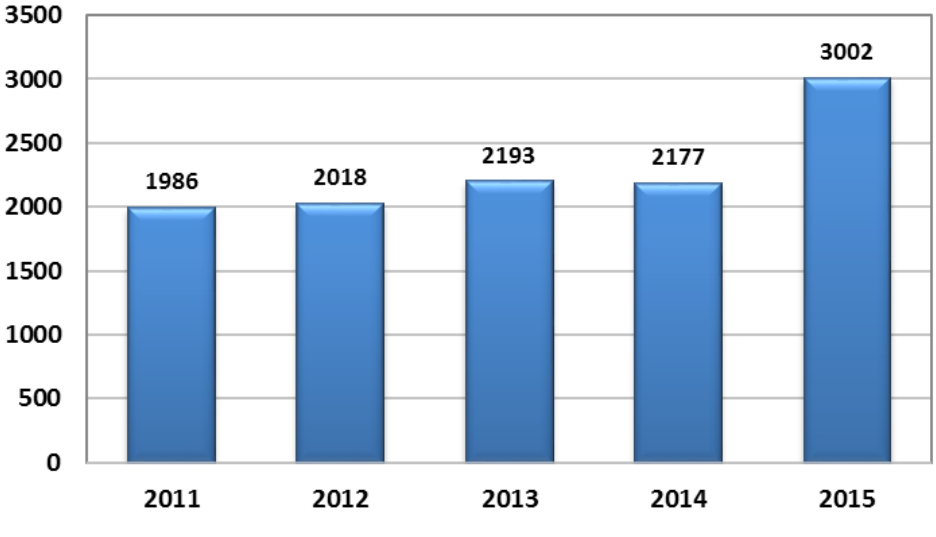

Fig. 1. The total number of counterfeiting incidents during the period 2011-2015 [6].

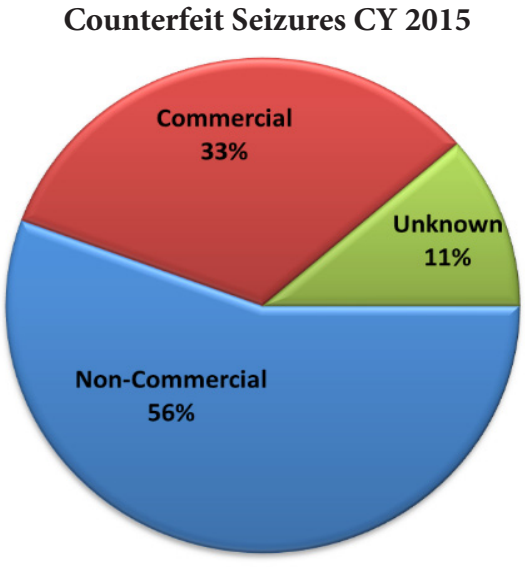

Fig. 2. Confiscation of Counterfeit Medicines, 2015 [6].

rectly through their transit through the territory of that country. If we analyze the crime incidence by continents (fig. 3), we see that the leader of counterfeit medicines is Asia – 1100 crimes, North America is ranked 2nd in the range with 779 crimes, followed by South America – 494 crimes and Europe with 358 crimes. Data were collected and analyzed by PSI.

If we consider the incidence of counterfeiting by therapeutic groups we see that the 3002 crimes that occurred in 2015 involved 1095 different pharmaceutical products. The number of products found in only one incident ranged from one drug to thirty-seven different drugs. The data showed that medicines for urogenital system, anti-infectives and for central nervous system are main therapeutic categories with the highest number of counterfeiting incidents. These three categories were determined as drugs most frequently subject to the pharmaceutical counterfeiting. While the ranks of the top therapeutic categories were relatively unchanged, the Institute has noted seven therapeutic categories that have had a percentage increase on a year-to-year basis. Specifically, the genito-urinary therapeutic category led with the largest percentage increase at sixty-five percent (+65%). Categories with percentage increases also included dermatologicals (+57%), cytostatics (+29%), cardiovascular (+29%), respiratory (+28%), CNS (+11%), and alimentary (+4%) (fig. 4) [6].

More and more people are buying drugs and medical devices over the Internet through online pharmacies and auction sites. Unfortunately, a large number of these Internet sites are not licensed and regulated and sell fake or substandard products.

If an online provider hides physical address, it is a warning sign that their products could be dangerous. WHO estimates that 50 percent of medicines available from such websites are counterfeit.

In particular, the purchase of drugs only on prescription from unlicensed or suspicious sources significantly increases the risk of getting substandard or fake products. It is important to consult a medical professional in order to obtain medicines from a regulated source.

Buying medicines online may seem cheaper, faster and more convenient, but the dangers are greater than the benefits [4].

In many countries it is legal to purchase drugs and medical products from authorized online pharmacies with a prescription if necessary. However, tens of thousands of websites provide drugs illegally. Combined with rising consumer demand, technological progress, namely the widespread use of the Internet, advertising, the sale and supply of illicit and counterfeit drugs through unauthorized and unregulated websites became a global and continually expanding problem.

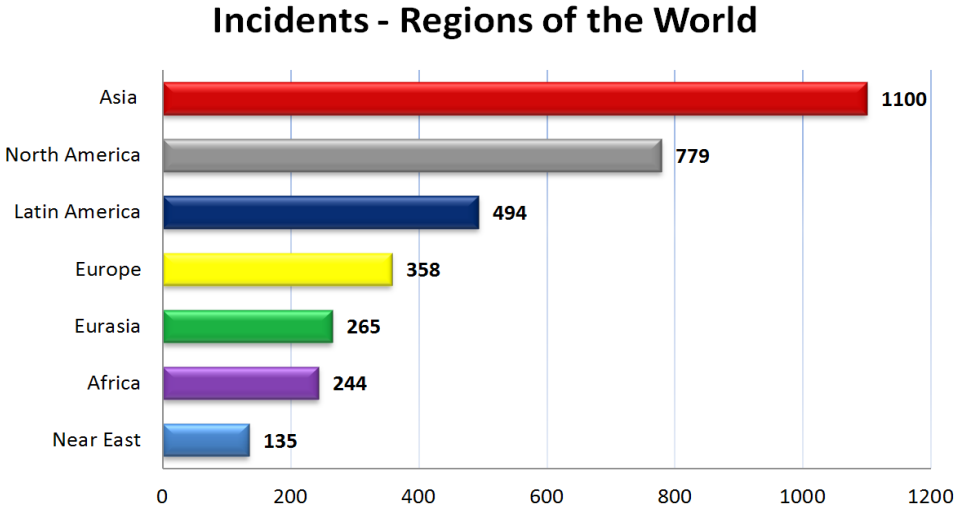

Fig. 3. The incidence of counterfeiting by continents, 2015 [6].

The report "A study of illicit online marketplaces" of Interpol analyzes the extent of the pharmaceutical delinquency problem on Darknet, through a case study of some of the largest online markets of counterfeit medicines: Silk Road 2.0 (which was later suspended by authorities of law enforcement) and Evolution Marketplace (which still works).

More than 10000 advertisements are posted in the section entitled "Medicines" on Silk Road 2.0. When we divide these numbers we find that the highest proportion of products published on Silk Road 2.0 refers to prescription medications. Rx drugs constitute 30 percent of the total amount of medicines advertisements on Silk Road 2.0, cannabis being the second product after its share – 17 percent (fig. 5) [7].

In order to lead a successful fight with continuously growing crimes, in 2011 was approved Directive 2011/62/EU of the European Parliament and of the Council of 8 June 2011 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, as regards the prevention of the entry into the legal supply chain of falsified medicinal products. This Directive contains rules concerning the extension of rules regarding sales agents, strengthening of intermediaries obligations, improvement of quality control of API and certain excipients, regulation of imported drugs intended for re-export and establishment of new rules on access to medicines stored in warehouses and free trade zones, demand of characteristics related to the safety of medicines prone for counterfeiting, strengthening of inspections and ensuring

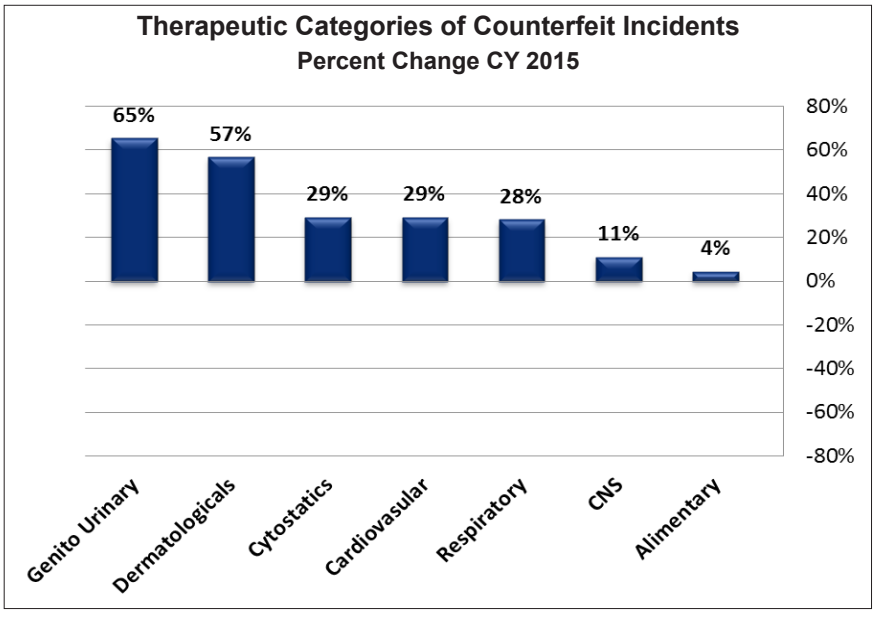

Fig. 4. Therapeutic categories of counterfeit incidents, percent change, 2015 [6].

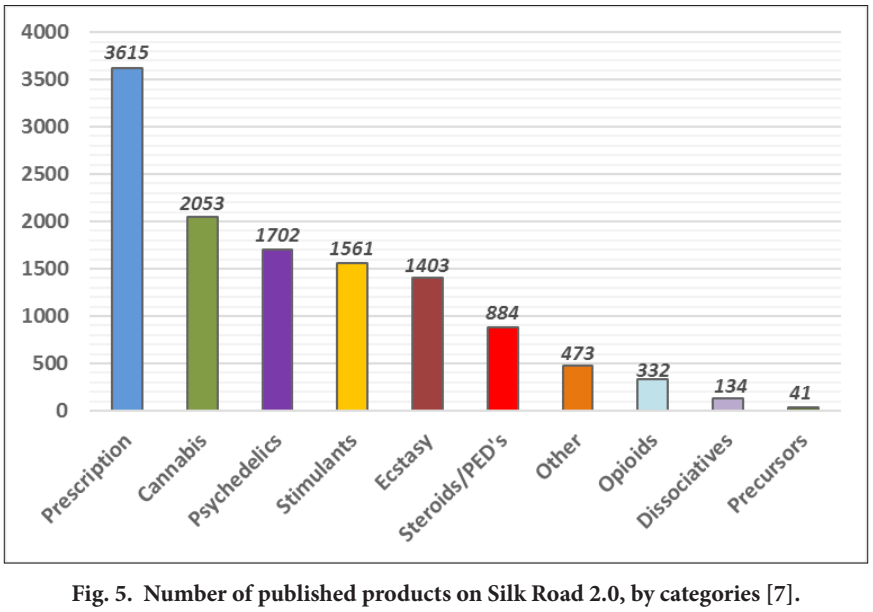

Fig. 5. Number of published products on Silk Road 2.0, by categories [7].

appropriate punishment for committing an infringement in the Member States [8].

The Council of Europe has been concerned by the lack of international law harmonization, deterrent penalties that were not proportionate to the harm caused to patients and the involvement of criminal organizations operating across borders. To this effect was approved "Council of Europe Convention on counterfeiting of medical products and similar crimes involving threats to public health", adopted in Moscow on 28 October 2011 (MEDICRIME Convention). MEDICRIME Convention is the first international criminal law instrument that obliges the states parties to criminalize:

- Manufacture of counterfeit medical products;
- Supplying, offering to supply and trafficking counterfeit medical products;
- Forging documents;
- Unauthorized manufacture or supply of medical products and the marketing of medical devices that do not conform to requirements.

The Convention provides a framework for national and international cooperation through various administrative sectors. It provides measures for coordination at national level, preventive measures aimed at public and private sectors, and measures to protect victims and witnesses. It also establishes a monitoring body responsible for tracking the implementation of the Convention by the States parties [9].

Open for seminars in 2011, the Convention has been so far ratified by 9 countries (Spain, Guinea, Hungary, Moldova and Ukraine) and signed by 26 other countries. The Convention was signed by Moldova in Vienna on September 20, 2012 and ratified on 14.08.2014 (Law no.67 of 16/04/2014 to ratify the Council of Europe Convention on counterfeiting of medical products and similar crimes involving threats to public health). MEDICRIME Convention came into force on 1 January 2016 [10, 11, 12].

The 65th Assembly of the World Health Organization, held in 2012 in Geneva, adopted resolution 65.19 that establishes the mechanism of fight against SSFFC Medical Products (substandard / spurious / falsely-labelled / falsified / counterfeit medical products) [13]. This resolution renewed and restored a mandate to WHO and Member States in addressing SSFFC medical products in a transparent and comprehensive way from public health perspective, and expressly excluded intellectual property rights. Its objective is to work with Member States to improve the quantity, quality and analysis of accurate data on SSFFC medical products and to use this data to better prevent, detect and respond to these products in order to protect public health [15].

Member States have adopted a work plan of SSFFC, containing 8 points, focused on cooperation, collaboration and consolidation of power.

The work plan of Member States SSFFC:

1. Strengthen the capacity of regulators and quality control laboratories.
2. Enhancing collaboration between regulatory authorities;
3. Communication, education and awareness;
4. Transparent collaboration of stakeholders;
5. Identify actions, activities and behaviors resulting from SSFFC medical products.
6. Increase the ability to strengthen national and regional integrity of the supply chain;
7. Cooperation regarding the supervision and monitorisation of the SSFFC medical products.
8. Collaboration within WHO regarding the access to qualitative, safe, effective and affordable health care products [13].

Global Surveillance and Monitoring System for SSFFC medical products was launched in West Africa, in July 2013. Since then, over 300 regulators from 113 member (fig 6) states have been trained in its use and 1040 SSFFC medical products have been reported [16].

Rapid Alert System for counterfeit medicines *(Rapid Alert System (RAS))* is a web communications network involving focal persons and representatives of countries and areas from the Western Pacific region, WHO and partner

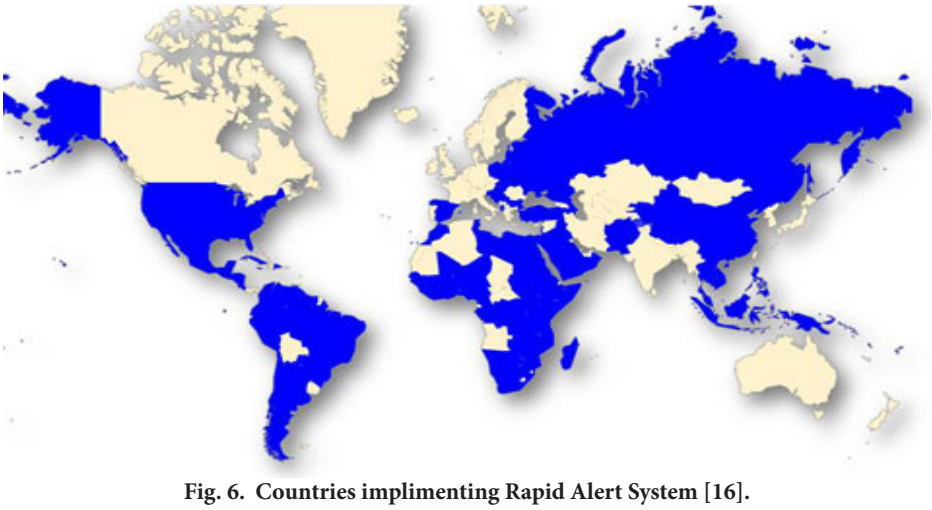

Fig. 6. Countries implimenting Rapid Alert System [16].

agencies. The aim is to warn countries, member areas and partner organizations, through focal points and representative network on cases of counterfeit medicines. Cases of counterfeit drugs can be reported through the system, using an electronic reporting form. Alternatively, reports can be submitted by any other means (e-mail or fax) to the secretariat, which will introduce immediately into the system [14]. Some Member States report suspected SSFFC medical products and other validated SSFFC medical products. Depending on the nature of the report, a moderator will disseminate information to all members of RAS. Confirmed cases are included in the database of WHO. When a report is received from WHO, it is loaded automatically into a secure database of WHO and immediately compared to all reports. WHO will contact the focal point of reporting within 72 hours for further details and if requested will provide technical support. In emergency situations this can take the form of facilitating emergency laboratory analyzes or in extreme and complex cases to send experts.

In all cases, analysts will work in focal point to gather more information about the possible SSFFC medical product in order to validate the information.

The analyst will close a case by classifying the SSFFC medical product in the following categories:

- Substandard
- Faked
- Genuine
- Not registered
- Stolen / diverted

This classification shall be carried out only if there is sufficient information to make a determination beyond doubt. During 2016 all focal points will be able to search the database through a secure link to verify if a suspected SSFFC medical product has already been reported to the WHO (fig. 7) [16].

All these are the main lines of fight against counterfeiting at national and international levels.

Interpol (International Criminal Police Organization) has a very large share in the fight against pharmaceutical crimes. This is an international cooperation organization of police forces. Created in 1923, the organization has 190 member states. It participates in combating counterfeiting of medicinal products through global and regional operations.

Operation Pangea is generally referred to as a global operation organized by Interpol in 2008 with support from the World Customs Organization and the Forum on International Crime in the pharmaceutical field. The theme of the annual operation is to combat online pharmaceutical crime and sale of medical devices. The Republic of Moldova, in collaboration with Medicines Agency and national law enforcement, participated for the first time in operation Pangea VIII in 2015. The conference in Brussels from 23-24 February was aimed at bringing together the contact points of 60 countries of the world participating in the following Pangea IX and 145 representatives from various national and global structures in this field.

Operation Pangea involves a week to prevent and combat the illicit sale of pharmaceutical products as well as medical devices online or in the market with the aim to guarantee the security of overall health and the health of patients, particularly vulnerable people: the poor, elderly, children and those sick. The problem of counterfeit and unauthorized drugs as well as medical devices is of worldwide importance. During this operation the customs, regulatory authorities of medicines and medical devices, national police and private sector companies (manufacturers and wholesale distributors) are working together. Its activity is directed towards three main components, which are used by illegal websites to develop commercial activ-

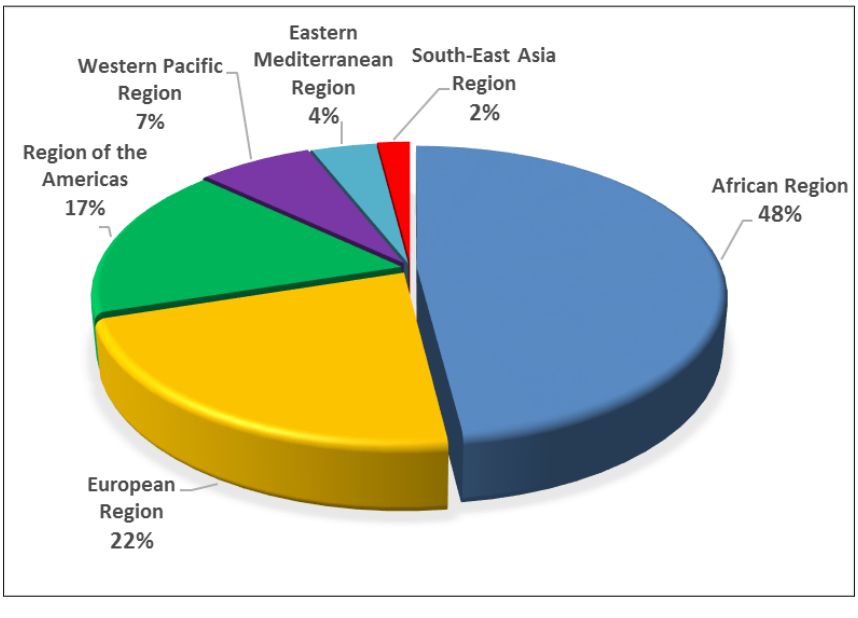

Fig. 7. Levels of current regional reporting, updated in March 2016 [16].

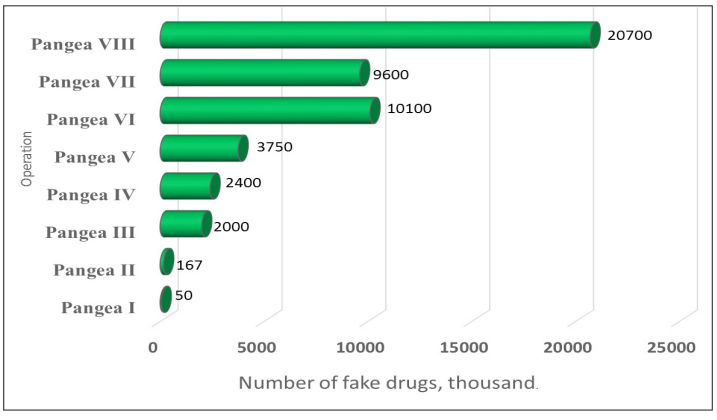

Fig. 8. The number of counterfeit medicines seized by INTERPOL [17].

ity – Internet Service Provider (ISP), payment systems and service delivery.

During the period 2008-2015 there were eight Pangea operations, 10 countries attended the first year and gradually their number grew in such a way that in 2015 there were 115 countries and representatives participating. The operation efficiency increases with the number of participants. During Pangea I operation several thousands of illegal medicines were seized, the number increased during operation Pangea II, so that in 2015 the number of seized drugs reached 20.7 mln (fig. 8).

Regional operations aim at disrupting the activities of transnational criminals involved in trafficking of illicit pharmaceuticals in the regions particularly affected by this problem, such as South-Eastern Asia (Operation-Storm) and all regions of Africa (e.g. operations Gibo, Mpili and Porcupine).

During the period 2010 – 2014, these operations led to the arrest of 1400 suspects, suspension of 57000 online illicit pharmacies and seizure of 30.3 million units of illicit drugs [17, 18].

Conclusions

1. The counterfeiting of pharmaceuticals is a global problem that involves several actors: institutions, law enforcement, customs, doctors, pharmacists, patients and citizens.

2. The competent national authorities in collaboration with the associations of doctors, pharmacists and patients must lead risk awareness campaigns regarding purchasing of pharmaceutical products from illegal sources.

3. Patients should be informed of the risks they assume by purchasing drugs from different websites.

4. The population should know that websites that sell drugs must have links directing to the competent national authority or the website of European Medicines Agency or Medicines and Medical Devices Agency from the Republic of Moldova.

5. Monitoring sites (and social networks) is vital in order to know the perception of patients about a brand or product. This monitoring is a source of information on trends in consumption and can highlight sites with counterfeits and illicit trade in real time.

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