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Risks Associated with International Trading of Medicines by Non-Licensed Entities and Non-Professionals

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Additional information is available at the end of the chapter

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Abstract

The making, distribution and trading of medicines can be traced back as far as antiquity. When talking about trading, sale or dispensing of medicines, it is almost impossible to separate this topic with the profession of pharmacy or pharmacists. Although most countries introduced legislations that put the trading of medicines largely in the hand of licensed businesses and professionals mainly pharmacists, informal and international trading of medicines and related substances has continued to be practiced in almost all countries due to loopholes in legislations among other reasons. This chapter highlights the risks associated with the trading of medicines by unlicensed organisations and non-professionals. These risks include the production and sale of counterfeit medicines, encouraging abuse and misuse of medicines, anti-competitive behaviour and so on. The major findings are that concessions made to allow non-licensed businesses and non-professionals to trade in medicines have resulted in several consequences that are threatening the whole world. It is this realisation that has prompted the recommendation that courage from decision makers is required for them to take a stand and hand over back the trading of medicines firmly in the hands of licensed professionals while outlawing loopholes that sustained the trade of medicines by unlicensed entities and non-professionals.

Keywords: informal, illegal, trade, medicines, non-licensed, non-professional

1. Introduction

The making, distribution and trading of medicines can be traced back as far as antiquity. The making, production or manufacturing of medicines, mixtures, admixtures and other dosage forms have been performed over the years by a wide categories of people including lay peo-

ple, priests, herbalists, traditional healers, midwives, medical doctors, nurses and pharmacists. As elaborated below, the practice of the art of healing was based on Arab, Egyptian, Greek and Roman texts, particularly those of Hippocrates, Aristotle, Dioscorides, Galen and others. The making of medicines was the domain of monasteries and local healers as medical training was not formalised then. The formal training and development of preparation techniques of medicinal mixtures based on standardised processes of harvesting, drying and distillation led to the abandonment of the old-fashioned herbal preparations practices by lay people who fell out of favour with the professionalization of the healing/medical community. But the distribution, sale as well as the local and international trade of medicines have been performed, in addition, by licensed and non-licensed people and businesses. This paper aims to describe and report on the risks associated with the trading of medicines by non-licensed business entities and non-professionals. In doing so, the paper elaborates on the reasons why international trade is prone to being conducted by unlicensed businesses and non-professionals, as well as on the sources of medicines traded.

In order to accomplish the above, the literature search, without any date limitation, was conducted to retrieve and include relevant articles published in English. The key words used were as follows: drugs, medicines, trading, illegal, informal, unlicensed and non-professionals. In the following pages, a brief overview on the historical perspective of the trading of medicines as a profession is presented. It is followed by a section elaborating on the trading of medicines by non-licensed and non-professionals. The remainder of the chapter is about issues specifically addressing the objectives of the paper as described above.

2. Trading of medicines as a profession

When talking about trading, sale or dispensing of medicines, it is almost impossible to separate this topic with the profession of pharmacy or pharmacists. From written history, it is established that the making, storing, supplying, issuing or selling and administration of medicines has been the prerogatives of people with combined skills of priest, physician and pharmacist. Earliest known prescriptions by Egyptians date as far back as 2700 B.C; documents such as the medical papyri of Kahun and Ramesseum [about 2040 B.C], the Edwin Smith and Hearst Papyri, the Lesser Berlin Papyrus [which dated from about 1600 B.C] and the Ebers Papyrus [about 1552 B.C] refer to medicines. On the Ebers Papyrus, there is a record of a formulary that listed about 700 medicines together with instructions on their compounding. Some of these medicines are still used today as excipients, adjuvants, solvents or active ingredients, such as alcohol [wines], acetic acid [vinegar], castor oil, myrrh, wormwood, aloes, magnesia, opium [source of narcotic compounds], peppermint, psyllium (Metamuci®) and many others [1, 2].

Similarly, the Chinese pharmacy (about 2000 BC)] as practiced by the Emperor Shen Nung who wrote the Pen Tsao or great/natural herbal, a manuscript that enumerated 350 medicinal entities with a distinction made about what is to be used by physicians and another for pharmacists. This is one of the old documents expressing the separation of duties between medical doctors and pharmacists long before the Palermo edit as explained below. With the constant change of balance of military conquests that saw alternative dominances and colonization

between African and European empires between the first and the seventh century AD, the Greek having gained the upper hand, their writings provide some more clarity on the practice of pharmacy [1–3].

During the first century AD, in his *Materia Medica*, Dioscorides listed 500 remedies prepared from plants, animals and metals. During the second century AD, it is Galen (130–201) who devised a system of pathology and therapy that ruled western medicine for over a thousand years. He wrote a compendium describing the preparation of medicines, thus earning himself the title of the “father of pharmacy” [3].

It should be noted also that the Arab physician, Rhazes (865–925 AD), wrote, in his “*Liber Continens*,” some of basic principles of pharmacotherapy such as “if you can heal with foods, then do not prescribe medicines.” Later on, Dr. Ali ibn Sina (980–1037 AD) wrote a medical reference book, “*Canon Medicinæ*” that summarised and expanded on principles of therapeutics and pharmacotherapy that have been influential from sixteenth to twentieth centuries [1–5].

It should be stated that throughout Europe, the roles of the physician, pharmacist and priest were intertwined. This threesome combination was and is still illustrative of the roles of custodians of medicines; namely, being able to determine what is wrong with a person; knowing what products should be used to treat what is wrong; and being compassionate for the well-being of the person with no financial incentive as primary consideration. It is the German Emperor Frederick II who, in 1231 AD, issued an edict known as the “Palermo Edict”. This legal document entrenched the separation of the practices of medicine and pharmacy, giving rise to the profession of pharmacy in Europe. In addition, this edict made provision for the official supervision of pharmacy practice and instructed pharmacists to prepare quality drugs according to their skilled art, in a consistent and standardised manner. This proclamation was followed by similar legislations in other parts of Europe; by 1408, the first Poison Acts was passed in Scotland by order of James I [1, 2, 6].

As Europeans explored the world, the Portuguese, Dutch and English navigators opened sea routes around the world with increased trading of diverse goods. By the fifteenth century, the trade in medicinal plants, health products and spices was a lucrative business that led to many conflicts between the Spanish, the Portuguese, the Dutch, the French and the British in their efforts to control the sources of these prized commodities [7, 8]. By the sixteenth century when Africa was finally made submissive, the ensuing massive slave trade went along with the demise of pharmacy in Africa but a growth of pharmacists as professionals in Europe and America [9–12]. As such, pharmacists known then as ‘apothecaries of the company of Grocers’ held the skills and knowledge on the preparations of concoctions, potions and other dosage forms due to several innovations as explained below [3, 13].

One major element of that growth was the production of reference books that became widespread occurrence after the invention of printing in Europe. The first attempt to standardisation was made in Florence [Italy] where the first official pharmacopoeia the “*Ricettario Fiorentino*” was produced in 1498, and a few years later was translated into Latin so that it could be used throughout Europe. The City of Nuremberg in 1529 was the first community to use a formulary legally binding on all apothecaries of that city [3, 14, 15].

Hence, during the sixteenth and seventeenth centuries, the art of the apothecary was developing rapidly in Europe such that in 1617, King James 1st of England granted the Apothecaries a royal charter which separated them from the Grocers. It is reported that the Grocers tried to resist, but the King stood firm as he saw the grocers as merchants having no professional skill, whilst the practice of the apothecary was an art practiced with skill and knowledge. By 1815, the Apothecaries Act of 1815 was passed. The net impact of the new Apothecaries Act was a clearer definition of the two professions, medicine and pharmacy [2, 3, 16–18].

3. Trading of medicines by non-licensed entities and non-professionals

The above brief historic overview served to show that the business of trading in medicines was largely into the hands of professionals. However, with the colonization of Africa, the loss of its manpower through slavery, the plundering of its resources and the demise of its major centres of learning in Egypt, Mali and other parts of the continent, the professionalization of pharmacy in Africa lagged behind in comparison to Europe, Asia and America [6, 19–21].

As illustrated above from the history of pharmacy in England, most European countries enacted legislation to place the trade of medicines in the hand of pharmacists and medical doctors; though informal trading continued unabated due to the lucrative nature of the trade, the loopholes in legislations and the recognition that herbal medicine practice was vested with some people through heredity and initiation but not academic training [22–25].

Nowadays, in Africa and South America, fraudsters posing as genuine traditional healers have exploited again the lack of regulation of traditional and herbal medicine practices to enter in disguise into informal trade of conventional medicines. They often buy medicines from legitimate outlets and repackage them and sell them [26, 27].

Moreover, the grocers and small traders of basic necessity goods are still the most common business entities from which people procure most household items including medicines for minor ailments. This situation results from regulatory concessions based on the classification of medicines in categories taking into account the probabilities of harm; with grocers being authorized to sell medicines deemed less harmful or over-the-counter drugs [27–30].

Hence, in Denmark, South Africa and several other countries, for instance, shops outside the pharmacy sector are allowed to or in some instances can obtain authorisation to sell over-the-counter (OTC) medicines that are suitable for sale outside pharmacies. In Denmark, it is the Danish Medicines Agency which decides whether a medicine can be sold at these shops; in South Africa, the Medicines Council establishes the list of Unscheduled Medicines suitable for sale outside licensed pharmacies. The staff employed at shops outside the pharmacy sector are not required to have a pharmaceutical education. The general mercantile shops are required to keep and sell OTCs as defined by the Danish Medicines Agency or the South African Medicines Council. These OTCs include products such as painkillers, cough suppressants, lozenges for a sore throat as well as nicotine chewing gums and some other remedies for the digestive system [31–34].

In Africa and South America, where most legislations were inherited from countries that colonised them, several countries had regulations on pharmacy similar to the ones of European countries. After independence, several countries continued to implement the Poisons Act or Pharmacy Act or Medicines Act until 1980s–1990s. It is during this period that several countries with the help of the World Health Organisation revised, updated or developed their pharmaceutical policies, regulations on registrations and sale of medicines, and the exercise of the pharmacy profession [35–40].

With the practice of traditional medicine well entrenched in Africa and Asia, the opportunities brought by the ease of packaging and transportation led to an ever-existing informal sale of medicinal plants, herbal and conventional medicines. Because the loopholes inherited from colonial laws still persists, informal trade of medicines and medicinal herbs on the streets and in non-licensed businesses is still a common sight in most African and other developing countries [41–44].

The practice known as informal trading or selling of medicines by unlicensed people and businesses is a widespread phenomenon facilitated by the lack of effective legislation, regulations and enforcement thereof. The international trade of drugs, medicines, chemicals and cosmetics both legitimate and grey markets have been and still is fuelled by financial gains. One of the underlying factors is the non-existing of formal trading outlets in some areas, particularly in urban slums and rural areas of most developing countries. During the end of twentieth century, unemployment has been also a driving force in the proliferation of informal trade of medicines; other factors will be discussed further [45–48].

The hallmarks of informal health products traders are that they have not been trained in pharmacy or any health-related professions and are not registered with any professional councils or regulatory bodies. Consequently, they are free agents whose sole motive to trade in medicines is to make money. Moreover, since the start of industrialisation in Europe, the subsequent decline in the formulation and preparation of medicines in community pharmacy outlets led to the transfer of the production or manufacturing of medicines in the hands of business entities owned by non-professionals or businessmen. As explained below, with the profit motive as primary consideration, this control of production and distribution of medicines by non-professionals has and still is a facilitating factor for the trading of medicines by non-professionals on the streets through the channels as explained below [49–50].

These businesses may be properly licensed to trade in medicines or cosmetics or other products; some may not be licensed but exploit loopholes in legislations to trade in medicines such as subcontracting companies and more recently as internet-based companies that are selling medicines. The characteristics of non-licensed entities are that they are not registered with regulatory bodies in the countries from which they operate, they are not run by professionals, and thus have no professional ethical allegiance. Like individuals, the sole purpose of these businesses is to make money from selling or trading health commodities and medicines without any consideration for the well-being of the people they sell their products to [51–54].

4. Why international trade of medicines is prone to illicit and unprofessional practices

The lack of professional ethics, compassion and concern for others is one of several considerations rendering international trade of medicines prone to illegal, illicit and unprofessional practices. Chief among the reasons is that fact that some countries, even, those with stringent medicines regulatory authority and control infrastructure, have legislated that medicines destined for export need not conform to legal requirements and standards laid down for medicines destined for their national or local consumption [55–58]. This discriminatory legislation which essentially tells manufacturers that their products that do not meet national standards should be exported is in itself one of the sources of substandard medicines that are flooding international trade. Indeed, when manufacturers know well that their products cannot be sold locally or exported to countries with strong quality control system, they will find unguarded outlets to do so [43, 59–61].

Parallel trade, a legitimate operation as explained below is often implicated as a potential way for illicit and unscrupulous counterfeiters to infiltrate the legitimate supply of medications as the medicines move between wholesalers and distributors after manufacturing and before reaching the last mile, or facilities dealing directly with end-users such as retail pharmacies, clinics and hospitals. Because of price differentiation based on the type of market, products available more cheaply in one market can be sold legally in another market at a higher price [36, 40, 45, 51, 62–64].

Hence, as medicines are shifted from market to market or more precisely from country to country, the original packaging and inserts in one language are replaced and repackaged with new ones in another desired language; in the process anti-counterfeiting features, such as holograms, are discarded entirely and legally so [57, 63, 64]. Worse, if the original packaging is not destroyed, it may be picked up by counterfeiters from landfills and reused. Thus, even countries with strong regulatory quality assurance system will be pried on this way as many legitimate pharmaceutical entities use parallel trade.

Parallel trading has been implicated also in the trading of counterfeit drugs. Several versions of fake Coartem®, an antimalaria product have been found in many African cities. Some seemed to have been manufactured for the African market as its packaging carried the logo of Nigeria's medicines regulator, the National Agency for Food and Drug Administration and Control—which is used as a seal of approval for authentic Coartem® throughout the continent. However, small details could have been noticed by a trained eye (**Figure 1**), in that the fake Coartem® in all three countries had an expiry date of 24 months instead of the usual 23 months for genuine Coartem®; some products had several languages errors; other versions had incorrect number of tablets in them [57, 65–69].

The above situation illustrates the consequences of the lack of oversight of the medicines supply chain by professionals such as pharmacists. This is why it is still another failure when some countries allow wholesalers that are not subjected to their pharmaceutical legislation such as general merchants, to import non-prescriptions drugs. These businesses that operate

without professional oversight by pharmacists may also fall prey to international criminal syndicates that may use their operations to add to their consignments other products including counterfeit drugs as explained above [59, 60]. Moreover, the weak capacity in developing countries at customs and the fact that the bribing of officials ensures that any consignment can enter a country facilitates the illicit trade [70].



Figure 1. Features differentiating fake and genuine Coartem®. Source: Newton et al. [56].

Most importantly, weak legislations and penalties facilitate illicit trade in medicines and counterfeit medicines. For instance, the penalty for manufacturing or distributing counterfeit drugs is very lenient in many countries. It is noteworthy that about 10 years ago, in Nigeria, a person convicted for such an offense faced an imprisonment periods ranging between 3 months and 5 years or had an option of paying a fine of 70–3600 US dollars. Similarly in some South American countries, the penalty for illicit trade or in drug counterfeiting was no more than six months in jail or an option to pay a fine [49–60, 62, 71–72].

The advent of internet-based businesses that cannot be inspected by pharmaceutical inspectors because of lack of physical storage facilities within the same location as the registered address of the business, the ease of reproducing original documents due to improved printing technology and the lack of quality assurance skills and systems in several developing countries, constitute some of the other factors that encourages the illegal international trade of medicines as well as the unfortunate existence of unscrupulous manufacturers and criminal syndicates [73–77].

5. Sources of medicines traded by unlicensed entities and non-professionals

Conceptually, at the core, medicines sold by unlicensed entities and non-professionals originate from either legitimate manufacturers or unlicensed, underground manufacturers (**Figure 2**). Legitimate manufacturers typically sell their products directly to primary wholesalers who will then sell to secondary even tertiary wholesalers depending on the architecture of the supply chain, the countries involved, the volume or quantities and types of products traded [51, 73].

As explained above, wholesalers may legally sell the OTC products to unlicensed retailers. From this point, unlicensed, informal traders can buy as much OTC products from the retailers due to lack of restrictions on quantities, on the conditions of transport or distribution of the products and most importantly, the non-application of restricting or controlling pharmaceutical regulations such as the mandatory registers to keep track of who bought what and how much. This is one of the most common ways that OTC and prescription products enter the informal trade and are sold on the streets of most developing countries [78, 79].

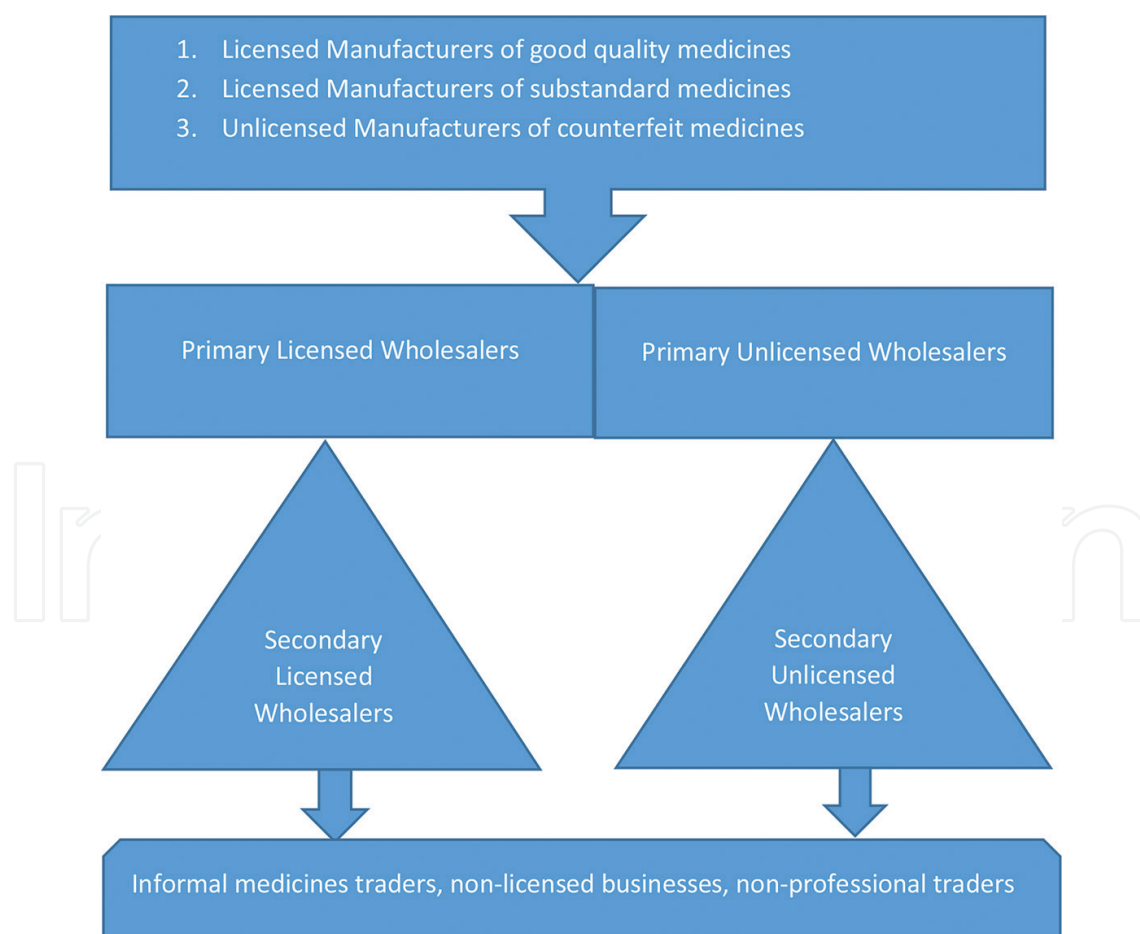


Figure 2. Sources of medicines traded by non-licensed businesses and non-professionals. Source: Author's illustration.

In the same vein, some unscrupulous legitimate manufacturers may knowingly sell their substandard products to primary or secondary wholesalers and even directly to retailers of countries with little or no established or well-performing quality assurance systems and through collusion or fraudulent practices get the products to informal traders who will then get hold of these products and sell them on the streets. Since informal traders have no means, knowledge or even interest in ascertaining the quality of the products they sell, this avenue gives unscrupulous licensed manufacturers to trade or get rid of their substandard products [41, 48–51].

As illustrated above, it goes without saying that unlicensed or underground manufacturers will use their primary unlicensed wholesalers to sale their substandard products or most commonly their counterfeit products. These products usually continue in the illegal, informal, criminal and fraudulent routes throughout until they reach the street vendors. It has been documented that counterfeit products may also enter the legitimate routes through corruption, collusion and fraud as explained below.

Basically, the entities involved may be a mix of legitimate and unlicensed entities as well as corrupt customs officials. In this collaboration of wrongdoers, consignments of the substandard and counterfeit products get included into legitimate purchases [59–60, 64, 70, 74]. This may be achieved by simply reproducing the legitimate documents and adding a “zero” to the original quantities ordered, and then supplying the difference. For instance, a legitimate primary wholesaler of a country A may have ordered 9000 Bottles of Aspirin 300 mg pack of 1000 tablets. The fraudsters will change the quantities to 90,000 × 1000 Bottles of Aspirin 300 mg, so they will add to such a consignment 81,000 bottles of 1000 tablets of Aspirin.

With corrupt officials at countries’ borders and the collusion with the primary wholesalers who initiated the purchase orders, the products will enter a country even if they were prohibited, or controlled drugs due to the absence of rigorous controls. As explained above during the procedures carried out as part of parallel trade, changes in packaging, relabelling and reconditioning provide opportunities for falsifying and counterfeiting even legitimate products [45, 62–65, 80–82].

Other sources of medicines sold by unlicensed entities are the stealing of legitimate shipments destined to wholesalers or retailers. This happens at seas or during road transport. Products from theft are generally genuine and of good quality at the time of their acquisition. However, due to incorrect storage, inadequate handling and improper transportation, their quality may deteriorate rapidly to the extent that by the time they reach the street vendors, they are already as good as impotent products. Several studies have reported how heat-sensitive medicines, notably, vaccines, antibiotics and anti-malaria products have been transported and stored in inappropriate conditions leading them to degrade [62, 66, 83, 84].

In some instances, travellers have been arrested for having smuggled in their luggage, prescription drugs destined for illegal and informal trade (see insert photo above, **Figure 3**). In other instances, qualified doctors have been forced to write prescriptions under coercion for controlled drugs that the criminals fill at the pharmacies and sell on the streets. Moreover, stealing also can be organised by criminals who approach healthcare professionals working

in hospitals pharmacies and other pharmaceutical outlets and thus obtain legitimate products that are subsequently sold to consumers through illegal and unlicensed businesses and outlets. It should be noted that non-professional healthcare workers or support staff members have been and are also a source of stolen products from health facilities. These products end up in the streets to be sold by unlicensed entities and non-professionals including legitimate or illegitimate traditional healers, herbalists, drug dispensers and other small traders [85–89].



Figure 3. Viagra® bust by South African customs officials worth ZAR 40 million [about 2.8 million USD] Photo: Patrick Aventurier/Gamma-Rapho via Getty Images. Source: <https://www.enca.com/south-africa/sars-biggest-viagra-bust>.

6. Risk associated with the trading of medicines by non-licensed entities and non-professionals

As explained above, the rationale trading in medicines by non-licensed businesses and non-professionals is to make a living, make money or make a profit from the legal or illegal sale of medicines. Indeed, as alluded to, some entities maybe licensed to sale legally medicines as in Denmark, South Africa and other countries. Due to the lack of a requirement for these businesses to record the transactions of medicines, a client may go through several grocery shops and procure as many painkillers or sleeping tablets for instance and get enough to use for suicide or to intoxicate their unsuspecting victims [30–33, 90]. The above illustrate the ever-present risk of the handling of small quantities of medicines by non-professionals. Several other risks exist as detailed below.

6.1. Criminality

6.1.1. *Acute criminal poisoning*

Several instances of acute poisoning have been reported as resulting from pharmaceutical products that have been disposed of unconventionally and irresponsibly by unlicensed entities and non-professionals. Most importantly, pharmaceutical, agro-chemicals and other products that have been involved in acute deliberate poisoning whether for suicide, parasuicide or with criminal intent have been acquired from the unlicensed street vendors [91, 92]. As explained above informal trading of medicines online or street-vending is unrestricted, uncontrolled and based on the sole purpose for the vendors to make quick money. Hence, even children may purchase these products indiscriminately. Other studies have reported underage patients having purchased prohibited substances including medicines and other substances from online, streets and from non-professional traders in Africa, Asia, Europe and elsewhere [90, 93–97].

6.1.2. *Production and distribution of substandard and counterfeit drugs*

As reported above, one of the major risks of unlicensed trading of medicines is that it fuels the criminal production and distribution of substandard, falsified and counterfeit medicines by criminal syndicates that operate in several countries. The World Health Organization (WHO) has defined counterfeit medications as products that are deliberately and fraudulently mislabelled with respect to identity and or source. The act of counterfeiting applies to products whether there are branded and generics; counterfeit products include products with the correct ingredients in insufficient dosing or quantity or quality; or with the wrong ingredient with/without active ingredients in insufficient amount or too much of it; or with products with fake packaging similar to the original product packaging. Furthermore, these products may often contain unlicensed analogues or mixtures of active ingredients that have not been evaluated for efficacy and safety in clinical trials; furthermore, their toxicity, pharmacokinetic, pharmacodynamics and drug interaction profiles have not been established [62, 63, 67, 98, 99].

The scale of the production is now a major concern to the international community because the proceeds of the sale of these medicines may be being used to finance other criminal activities including terrorism. It is estimated that illegal trading of drugs may have generated US \$531.6 billion in 2013 [100]. The range of counterfeit products reaching markets is broad including fast-moving OTCs, generics as well-branded high-tech products. It is estimated that in more than 50% of cases, medicines purchased over the internet from illegal sites that conceal their physical address have been found to be counterfeits [101]. The type of counterfeit drugs most frequently faked in developing countries are medicines used for infectious diseases such as antibiotics and anti-malarial products. Counterfeit antimalarial drugs are widespread in developing countries, particularly Southeast Asia and Africa; hence, even fake antiretroviral drugs have been reported in Africa. In developed countries, drugs used for chronic conditions such as anticancer, lipid lowering drugs, anti-allergic, endocrine agents (both hormones and steroids), as well as drugs for the erectile dysfunction predominate. With regard to Viagra®, results from analysis of recovered samples showed that only 14% of the samples had been authentic; and of the 626 UK samples, 83% of these samples were counterfeit [102–109].

6.2. Price increase and unfair competition

The sale of medicines by unlicensed vendors results in several anti-competitive behaviours. On one hand, for most prescription drugs, the prices of these drugs sold on the streets at less than half their normal prices. This is the chief reason that pushes consumers to buy these products as they believe to be saving money by buying from the streets in comparison to how much they would have paid from pharmacies. It is well-established that substandard products are generally cheaper than genuine products. On the other hand, for products that contain ingredients with addictive properties such as codeine, the prices of these products on the streets are up to 1000 times more than their normal prices in pharmacies [110–114].

Due to patents and intellectual properties' infringements, there are economic risks quantifiable in loss incurred by legitimate retail businesses licensed to trade in medicines. Several legitimate companies are deprived of their rightful profits due to the unjust competition from unlicensed businesses and non-professionals [115, 116].

The financial loss resulting from counterfeiting of medicines is huge and appears to be increasing annually. Estimates from WHO are that about 32 billion US dollars were lost to drug counterfeiting business in 2004; increasing to 40 billion US dollars in 2006 and it was expected to reach 75 billion US dollars by 2010 [110, 117].

It should be remembered that every dollar spent on buying a medicine from an unlicensed entity, it is a dollar lost by a legitimate business that is paying taxes to the government. Most importantly, every dollar spent on a substandard medicine is money lost by the consumer that should have been used to buy a genuine medicine that has some guaranteed potential of healing rather than the high probability of harm from counterfeit product or a product not stored in appropriate conditions.

6.3. Promotion of abuse and misuse of medicines

Unlicensed traders of medicines and non-professionals promote the abuse and misuse of medicines by increasing the availability, accessibility and sometimes affordability of prescription and non-prescription drugs. By making it easier for people to get the medicines without any control, these traders facilitate to feed the habits of people affected by the abuse condition [118–121].

It should be noted that drug or medicine misuse refers to the use of a drug for purposes for which it was not intended or using a drug in excessive quantities; drug abuse is the misuse of prescription or over-the-counter drugs with negative consequences such as addiction, decreased performance at work, and or with problems at work, school, home or in interpersonal relationships or problems with the law. People misuse or abuse OTCs and prescription drugs as a result of being previously given them for a specific ailment or by being influenced by friends or family members [120–123].

The cycle of abuse may start because getting a prescription means paying a private practitioner or a prescriber or spending time in long queues at public health facilities; people make a shortcut by buying from the streets. Because people continue to buy, informal traders or

unlicensed entities feel vindicated to acquire more stock for their clients. This situation in turn encourage the middle suppliers and ultimately the manufacturers or criminals to get the stock or manufacture these substandard or counterfeit medicines in order to meet the needs for their niche markets [124].

The most common medicines abused are codeine-based (especially compounded analgesics) medicines, cough products (particularly containing dextromethorphan), sedative antihistamines, decongestants and laxatives as well as medicines used to increase or decrease appetite; to enhance sexual performance such as Viagra® and antibiotics. Of great concern is the abuse of opioids or narcotic drugs that are controlled drugs normally obtainable only with a prescription. Given the addictive properties of these medicines, patients sometimes pressurise their healthcare providers to prescribe these products to them, hence triggering the cycle of abuse [125–127].

6.4. Antibiotic resistance and treatment failure

One of the most damaging consequences of informal trading of medicines is the widespread facilitation of the misuse of antibiotics as unlicensed traders make them available to the general public. The unrestricted use of antibiotics combined with the diminished quality or potency of products sold due to improper storage conditions create an environment ripe for the onset of antibiotic resistance. Furthermore, counterfeit antibiotics with low amount of actual active antibiotics or worse with no active ingredient at all are even more dangerous for three reasons, and they provide false assurance and hope to the sick people who believe that they are being treated; they thus delay the actual treatment and thus provide the germs the time to multiply and aggravate the condition; and finally, if in low doses they provide the germs with the means to develop resistance. It is documented that resistance to malaria medicines, anti-tuberculosis, antiretroviral drugs and other infections has resulted from such instances [116, 128, 129].

It goes without saying that the ultimate outcome will be treatment failure. Some experts believe that germs' resistance stemming from substandard, falsified and counterfeit drugs has contributed a lot to the current stalemate in the fight against malaria and tuberculosis in developing countries. Furthermore, when treatment failure is experienced by patients after using medicines they got from public health facilities, it leads them to lose confidence in the healthcare system and sadly this forces them to resort to alternative sources of drugs including informal market or alternative treatment modalities including traditional medicine which is also ill-equipped to deal with deadly diseases such as malaria, HIV and tuberculosis. Hence, it is not surprising that an estimated 700,000 deaths per year are believed to be caused by fake antimalarial and anti-tuberculosis products [130–136].

6.5. Adverse drug reactions

Adverse drug reactions (ADRs) leading to hospitalisations have been reported as a result of the consumption of medicines obtained from non-licensed businesses and non-professionals. Although the advent of ADRs is a normal occurrence even when using legitimate drugs, informally obtained drugs carry added risks due to improper storage, uncertain quality, and incorrect use as a result of the lack of professional oversight [137–139].

6.6. Fatalities

Several fatal cases have been documented resulting from the consumption of medicines of dubious quality brought from unlicensed entities. Reports of acute poisoning resulting from counterfeit, adulterated, substandard or falsified drugs abound. Hundreds of deaths from acute renal failure due to poisoning from diethylene glycol in cough syrups have been reported in Haiti, Bangladesh, Nigeria, India and Argentina. The following cases illustrate the range and scale of circumstances in various countries. In Pakistan, 107 people died as a result of consuming a contaminated product made of isosorbide and very high amounts of pyrimethamine. In Niger, about 2500 people had died following the administration of counterfeit meningococcal-vaccines (containing no active ingredient) that was administered to some 60,000 people during the 1995 meningitis epidemic. In China, by the end of 2001, about 192,000 people were reported to have died as a result of the utilisation of fake medicinal products. Furthermore, in 2007/2008, a tainted Chinese crude heparin product killed 149 persons in 11 different countries including 81 deaths in the USA [140–158]. The above suggest that several other deaths due to products traded informally by unlicensed entities and non-professionals go unnoticed, unreported and unaccounted for.

7. Suggested strategies to mitigate risks associated with illegal and informal trade of medicines

The scale of the consequences from illegal and informal trading of medicines by unlicensed businesses and non-professionals ought to galvanise a resolve and a strong response from the international community of nations. Several international resolutions and initiatives have been implemented as far back as over two decades ago with a focus on counterfeiting. Given the trajectory that the business of counterfeiting and its associated spin-offs such as terrorism, it is time to rethink the concessions that were made by parliamentarians of several nations to take out the control of the trade of medicines from pharmacists or more specifically from their national pharmaceutical regulatory controls [159–163].

Everyone agrees that medicines are not ordinary commodities; the fact is that most of them are potent at doses expressed in milligrams, that is, in very small quantities; their abuse brings too much suffering and problems to society. On the contrary, when appropriately managed, controlled, prescribed, dispensed and used correctly, they relieve mankind of many of its diseases, suffering and thus contribute to happiness, the ultimate search for every soul on the planet earth.

Although several strategies may be and will be suggested to address the risks and consequences of illegal international and national trading of medicines, none requires more courage from decision-makers than taking the stand and saying that ‘enough is enough’. The trade of medicines should be professionalised and regulated in such a way that the illegal trade will scare most amateurs trying to get into it; that street-vending of medicines will not only be outlawed but completely eliminated as it is made to be unproductive and unsustainable [164, 165].

The courage needed to address the consequences of illegal trading of medicines should be great as the courage that the world summoned to establish the United Nations, the Global

Fund and other institutions that have made a difference to the world. What is really said here is that the fight against illegal trading of medicines as well as the production and sale of drugs of abuse should be a top priority for ministries of health, finances and justice of nations of the world [140, 166]. The belief that current and existing national and international interventions suffice to handle this problem is clearly contradicted by the facts on the grounds.

The situation demands that some innovative ways should be found and a rethink of the interventions already implemented. Some suggestions are given below.

7.1. Going back to basics—restoring the mandate of trade of medicines to professionals

There should be a concerted effort from international trading blocks and institutions to support their constituencies to revise, review, amend or update their legislations and/or regulations in order incorporate with no ambiguity the stand that 'no one will trade in medicines unless he is properly licensed with a verifiable physical address and meet criteria defined in existing good practices governing the procurement and sale of medicines in international trade'. This should also include specific regulations on maintenance of traceability of all categories of finished medicinal and health products as well as of excipients and other raw materials used in the production of medicines.

7.2. Revamping national and international legislations—outlaw double standards

The double standard entrenched in several national legislations that essentially allow national manufacturers to export their substandard products to other countries should be repelled. Moreover, parallel trade, which is one of the causes of foiling of traceability of products as a result of manipulations legally permissible, should be revised with clear instructions and legally binding standards to ensure that the traceability of the products and their sources is maintained.

7.3. Implement severe punishments and penalties

Concurrently, punishments and penalties for infringements should exclude options for paying fines but increase the harshness of penalties as deterrent. Furthermore, international cooperation and collaborative investigations on existing criminal syndicates, sharing of related information between law-enforcing agencies should be enhanced.

7.4. Encourage local production and strengthen national QA systems

Put in place mechanisms to encourage priority local production of products that lend themselves to local production because of the existence of raw materials and skills base; and mechanisms that foster quality assurance systems strengthening in countries with weaker systems. Foster a good neighbourhood culture that discourages undue and unfair competition but supports collaborative efforts that ensure accessibility and availability of good quality medicines. Most importantly, all countries should establish market surveillance through their scientific institutions, academia and/or with the assistance of legitimate manufacturers who are willing to be involved in the fight.

7.5. Online pharmacies to be restricted to defined territories and prohibited to trade internationally

As extreme as it sounds, the experience of the past decades have shown that oversight of online pharmacies' operations has proved difficult. Although, the suggested restrictions might not be implemented by concerned pharmacies, the key here is that the enforcements of heavy penalties when deviations have been uncovered is what is sought here.

7.6. Robust, unrelenting and consistent public health education campaigns

There is a need to develop educational materials with clear messages targeting public health officials and health care practitioners, customs' officials, the youth and consumers at large, on the dangers of inappropriately stored, substandard, falsified or counterfeit products; as well as on how to identify quality marks on genuine products. The campaigns should be launched in various media including national theatrical performances, radios, television and newsprints.

7.7. International blacklisting of rogue, unscrupulous and non-conforming manufacturers, wholesalers and distributors of medicines

It is suggested here that, just as there is an international database of clinical trials, an international database of companies, businesses and entities that have been confirmed as aiding, assisting, contributing to the trade of substandard, falsified and counterfeit drugs or practicing outside the regulatory limits of good practices, should be instituted as a way of shaming these enterprises and alerting buyers not to buy from or trade with them.

8. Concluding remarks

This review has highlighted the origins, the rationale and the risks associated with the trading of medicines by unlicensed organisations and non-professionals. These risks include the criminal poisoning, the production and sale of counterfeit medicines, unfair competition, encouraging abuse and misuse of medicines, and treatment failure as well as fatalities. The major findings are that concessions made to allow non-licensed businesses and non-professionals to trade in medicines have resulted in several consequences that are threatening the whole world. It is this realisation that has prompted the recommendation that courage from decision-makers is required for them to take a stand and hand over back the trading of medicines firmly in the hands of licensed professionals while outlawing loopholes that sustained the trade of medicines by unlicensed entities and non-professionals.

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