Dermatologic Consequences of Substandard, Spurious, Falsely Labeled, Falsified, and Counterfeit Medications

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KEYWORDS

• Counterfeit drugs • Drug eruptions • Substandard drugs • Fraud • Crime • Pharmaceutical preparations

KEY POINTS

- Substandard and falsified medications are a global problem, leading the World Health Organization to estimate that up to 10% of medications worldwide are counterfeit, fraudulent, or falsely labeled.
- Quantitatively or qualitatively irregular pharmaceutical products affect individuals, families, communities, and entire populations by weakening primary prevention of disease and secondary containment of disease; permitting the rise of drug resistant pathogens; creating vulnerabilities to overdose or poisonings; and directly causing adverse reactions.
- One way for substandard or falsified medications to become available in the United States is via improper or illegal importation but it is often difficult to distinguish these products from authentic ones.
- Determining the cause of a suspected drug reaction is particularly challenging when the culprit is an unidentified and entirely unsuspected adulterant, contaminant, or substitution.

INTRODUCTION

The perception among most Americans is that federal agencies tightly regulate the production, packaging, distribution, and sale of pharmaceutical products. As a result, people generally believe that prescription medications are, for the most part, safe and effective. Admittedly, segments of the population may undergo temporal waves of uncertainty and suspicion, but this sort of hesitation usually dissipates under circumstances of dire illness.

Although generally favorable perceptions apply to medications regulated by federal agencies, many products, including dietary supplements and homeopathic remedies, are underregulated, and often come close to being unregulated.

Presented in part as an invited lecture at the International Congress of Pediatric Dermatology, July 2017, Chicago, IL.

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Dermatol Clin 40 (2022) 227–236

https://doi.org/10.1016/j.det.2021.12.008

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Table 1
Governing bodies differ in their classifications of counterfeit drugs

FDA[1]	Centers for Disease Control and Prevention[2]	WHO	Interpol[3]
Counterfeit/fake	Counterfeit/fake	Substandard/out of specification	Fake
Spurious		Unregistered/unlicensed	Stolen
Substandard		Falsified	Illicit
Falsified			Counterfeit
Falsely labeled			Falsified
			Diverted
			Smuggled
			Trafficked
			Expired

Current federal legislation enables many dietary supplements and homeopathic products to evade serious scrutiny for safety and efficacy.

In the United States, the Food and Drug Administration (FDA) and other agencies regulate safety and efficacy of pharmaceutical products and establish standards for manufacture or importation. Similarly, most nations and many international organizations have their own regulatory structures. But a parallel universe of fraudulent products, including treatments for common dermatologic conditions, exists with the *raison d'être* to evade the scrutiny and costs of regulatory adherence.

Nevertheless, some products, such as drugs and biologics that are fully regulated by federal agencies, may reach the public with various irregularities. In plain terms, two general types of irregularities exist: quantitative and qualitative. Quantitative irregularities manifest as either *too much* or *not enough* of the professed medication. Qualitative irregularities, however, are myriad and defy such simplification. Products can be contaminated, adulterated, substituted, or mislabeled, among other transgressions, all of which add to burdens of disease and costs to society. The World Health Organization (WHO) and the FDA have official terminologies to categorize counterfeit medications (**Table 1**). For example, the FDA uses the description *substandard, spurious, falsely labeled, falsified, and counterfeit (SSFFC) medical products*. Although the WHO uses different terminology, in this article we use SSFFC to encompass the entire range of products associated with some sort of fraud, deception, evasion, or criminality involved with bringing the product to public use.

In global pharmaceutical markets, the scale of counterfeit and otherwise fraudulent medications is staggering.[4] Approximately 10% of pharmaceutical products worldwide (approaching 30% in parts of Africa, Asia, and Latin America) are substandard in ways that are both lucrative and criminal. On a per use basis, fraudulent medications cause more adverse events than legitimate preparations and contribute to approximately 100,000 deaths/year worldwide. The entire problem is accelerating alongside the COVID-19-pandemic.[5]

All health care providers should be aware that these problems exist and also that they are increasing in the United States and abroad. The dermatology community has an important but ill-defined role in fighting this problem, especially by detecting suspicious products from their cutaneous side effects and then reporting the events. In this article, we describe the worldwide scope of the problem, discuss dermatologic consequences of such medications, and offer recommendations to help dermatologists respond to this public health issue.

Dermatologists in particular must be cognizant of the pervasive nature of SSFFC medications, given the frequency of cutaneous drug reactions and the extreme risks associated with severe drug reactions (eg, toxic epidermal necrolysis or drug reaction with eosinophilia and systemic symptoms). Determining the cause of a suspected drug reaction is particularly challenging when the culprit medication is an unidentified and entirely unsuspected adulterant, contaminant, or substitution.

Recognizing irregularities in the production of legitimate (ie, approved) drugs (as well as illicit drugs) is a public health issue of increasing importance, one that adds to the burdens of disease and costs to society. The introduction of counterfeit, contraband, and substandard medications can cause unanticipated adverse outcomes that affect the health of individuals, including untreated illnesses, prolonged suffering, drug overdose, adverse drug reactions, and death; but can also affect the health of populations by generating

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drug-resistant pathogens and failing to control the spread of disease.

In this article, we discuss SSFFC medications, the drug reactions they may cause, their effects on society, and ways to report possibly suspect products to the proper authorities. When possible, we emphasize aspects of the problem that affect children to conform to the scope of this special pediatric-focused issue of *Dermatologic Clinics*.

TERMINOLOGY

Until 2017, the WHO applied the label SSFFC for a wide range of medication irregularities.[4] In 2017, however, the WHO changed the collective label to substandard and falsified medical products[5] and created three subgroups: (1) substandard, (2) unregistered/unlicensed, and (3) falsified medical products (see **Table 1**).

Substandard, also called *out-of-specification*, products are "authorized medical products that fail to meet either their quality standards or their specifications, or both." *Unregistered/unlicensed* products are those that have "not undergone evaluation and/or approval by the National or Regional Regulatory Authority (NRRA) for the market in which they are marketed/distributed or used, subject to permitted conditions under national or regional regulation and legislation." Lastly, *falsified* medical products are those that "deliberately/fraudulently misrepresent their identity, composition or source." However, the FDA continues to use the WHO's older SSFFC terminology (**Table 2**).[1]

METHODS

To determine the extent and scope of the problem relating to dermatology worldwide (not just in the United States), we searched MEDLINE for examples of SSFFC products that were used to treat dermatologic conditions or that caused an adverse cutaneous drug reaction. Our goal was to find representative or instructive examples of each type of dermatology-related SSFFC category, not to exhaustively identify every documented case in the literature.

The key element in our search strategy was selecting MeSH terms that are associated with SSFFC medications. Using MeSH hierarchies available at www.ncbi.nlm.nih.gov/mesh/, we developed this strategy and searched via the OVID interface with MEDLINE, limiting the search to case reports and review articles published after 1946: *exp** (*exp* preceding a MeSH term indicates the term was used in its "exploded" form). Fraud/OR *exp* Prescription Drug Diversion/OR *exp* Substandard Drugs/OR *exp* Drug Trafficking/OR *exp* Counterfeit Drugs/OR *exp* Drug Contamination/OR Drug Industry/es,lj,st OR Pharmaceutical Preparations/st OR (*exp* Nonprescription Drugs/AND (Internet/OR Commerce/)). To narrow the list further, we used the Boolean AND function for (exp Dermatology/or exp Skin/or exp Skin Diseases/or exp Skin Neoplasms/or exp Skin Physiologic Phenomena/or exp Skin Manifestations/or exp Skin Abnormalities/).

Next, we examined the titles (and abstracts, if available) to identify relevant articles. We obtained and reviewed papers written in English, French, or

Table 2
Definitions as specified by the FDA[6]

Term	Definition
Substandard/out-of-specification	Products are proper pharmacologic products produced by manufacturers authorized by the National Medicines Regulatory Authority, although the specific products do not meet national quality specification standards.
Spurious drugs	Manufactured under a name of another drug, imitate another drug, or have been substituted wholly or partly by another drug. Spurious drugs thus conceal the true pharmacologic identity of the product or formulation. Spurious drugs generally resemble well-known brands in some way, but nevertheless conceal the true identity of the product or formulation.
Falsely labeled drugs	Genuine products with false packaging.
Falsified drugs	Produced criminally with fraudulent intent.
Counterfeit drugs	Drugs entail the deliberate attempt to imitate a genuine product; therefore, counterfeit medications are fakes intended to imitate a genuine product.[3]

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Spanish. In addition, we perused each paper's list of references to uncover other potentially relevant publications.

RESULTS

Our search strategy produced a list of approximately 500 indexed papers, not all of which were relevant for the purpose of this article. We selected about 20% of the papers to review in detail and describe types of SSFFC-induced adverse effects in **Table 3**. In addition, we provide several instructive examples of dermatologic side effects of these products.

Case Study of Unregistered/Unlicensed Medications

One example involves cases of fixed drug eruptions caused by a contraband medication in a community of Salvadoran-American children in the Washington, DC, area. Several children presented with recurrences of unexplained blisters in fixed locations. We learned they had taken a

Table 3
Case examples of fraudulent medications (based on WHO classification)

Flaw in Medication	Example or Event	Consequence (Dermatologic or Other)	Location and Year
Substandard			
Bacterial contaminants	Desiccated placenta	Infant infection with Group B streptococci	Oregon, 2016[6]
Fungal contaminants	Methylprednisolone contaminated with fungi	Meningitis, epidural abscess, vertebral osteomyelitis, diskitis, phlegmon, arachnoiditis	Michigan, 2012–2013[7]
Heavy metals contaminants	Kelp supplements contaminated with arsenic	Memory loss, alopecia, rash, fatigue, debilitating nausea/vomiting	California, 2007[8]
Organic contaminants	L-tryptophan sleep supplements contaminated with di-tryptophan animal of acetaldehyde	Eosinophilia-myalgia syndrome	United States, 1985–1989[9]
Falsified			
Adulterated with corticosteroids	Topical steroids in Chinese cosmetics Clobetasol in "Asian herbal" compounds for atopic dermatitis Prescription-strength betamethasone purchased over the counter from African-wares store	Steroid-induced rosacea-like dermatitis Steroid atrophy Discontinued before adverse effects	China, 2017[10] Washington, DC, 2017[11]
Adulterated with antibiotics	Traveling peddlers selling medications containing cotrimoxazole	Fixed drug eruption	Republic of Congo, 2005–2008[12]
Unregistered/unlicensed			
Medication licensed abroad but not in United States	Baczol cold medication containing cotrimoxazole	Fixed drug eruption	Washington, DC, 2017[13]
Preparations purchased online	Bleaching creams	Chemical burns	California, 2015[14]

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cough and cold medication called Baczol Antigripal[13] manufactured in El Salvador. The product contains a sulfonamide antibiotic, trimethoprim-sulfamethoxazole, which is available over the counter in El Salvador but requires a prescription in the United States. Although the box stated (in Spanish) that sale was permitted only in El Salvador and required a prescription, the patient's families bought these products without prescriptions at Hispanic grocery stores in the Washington, DC, area.

In 2013, a team investigated the availability of Baczol products and found them for sale without prescription in 7 of 19 Hispanic grocery stores in DC, Maryland, and Virginia, despite an existing FDA import alert that prohibited their sale in the United States. Trimethoprim-sulfamethoxazole has many serious adverse effects including toxic epidermal necrolysis, Stevens-Johnson syndrome, nephrotoxicity, bone marrow suppression, and benign cutaneous hypersensitivity and photosensitivity reactions.

Case Study of Falsified Medications

Patients may develop signs of topical steroid overuse after treating such conditions as atopic dermatitis with adulterated products. For example, many patients at the pediatric dermatology clinic at Birmingham (UK) Children's Hospital reported good results from treating their atopic eczema with over-the-counter "herbal creams." The investigators analyzed 24 creams submitted by 19 patients and found clobetasol propionate, clobetasone butyrate, betamethasone valerate, and other potent-to-ultrapotent corticosteroids in the purportedly "herbal" products.[15]

Another report describes the pervasive presence of topical steroids in Chinese cosmetics.[10] These adulterated preparations, marketed as safe herbal folk remedies, can lead to serious dermatologic and systemic complications.

Finding products labeled as "herbal" but adulterated with pharmaceuticals and even with animal parts (quite the opposite of herbal) is well-described. One paper describes a nationally distributed "herbal" product whose label listed 17 bovine organs among its ingredients, including brain, spleen, lung, liver, pancreas, pituitary, pineal gland, adrenal glands, lymph node, placenta, prostate, heart, kidney, and intestine.[16,17] That paper suggests that customers may be unfamiliar with, and therefore misunderstand, ingredient names, such as orchis, which means the substance was derived from testicles, not orchids. Nevertheless, the product was sold at a nationwide chain as an "herbal" dietary supplement.

These examples of products labeled as "natural" yet containing ingredients ranging from bovine testicles to illegal amphetamines, highlight the medical and social implications of such adulterated products. Consumers should be reminded that products marked as "natural supplements" are often wrongly perceived as inherently benign and therefore dismissed by the public as "safe" and free of potent drugs and medications.

Case Study of a "Nonexistent" Medication

Paradoxically, the absence of an expected medication can lead to cutaneous adverse events. An instance of a reaction caused by a "nonexistent" medication arose in preterm infants born less than 24-week gestation, who developed unexplained erosions (on perianal and perioral surfaces) and blisters (on dorsal hands and feet).[18] All affected infants were on total parenteral nutrition that was later determined to lack supplemental zinc, leading to a classic presentation of zinc-deficiency disorder. This situation was the consequence of a national shortage of injectable, sterile, parenteral-grade zinc that is a necessary component of complete parenteral nutrition preparations. The observation was reported to the FDA, who issued an immediate nationwide alert. The Centers for Disease Control and Prevention found similar cases at other neonatal intensive care units; however, the problem was soon corrected with restoration of the supply of parenteral-grade zinc.[18]

Case Study of a Substandard Medication

Commercially available medications and supplements may not always meet quality specifications set forth by regulatory agencies. For example, a 54-year-old woman presented to an occupational medicine clinic with a 2-year history of alopecia and memory loss.[8] A urine sample revealed an arsenic level of 83.6 μg/g of urinary creatinine (normal <50 μg/g creatinine). Her symptoms were caused by arsenic-contaminated kelp supplements, which she took daily. The investigative team then measured arsenic levels in several commercially available kelp supplements and found arsenic levels exceeding FDA limits in eight of nine samples obtained from local health stores.[8] The case report did not comment on the source or reason for the contamination. Other published reports indicate that arsenic-contaminated dietary supplements are manufactured most commonly in China or other East Asian nations, which is similar to the situation with a vast range of products contaminated with heavy metals .

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These examples represent some of the dermatologic problems associated with SSFFC products. **Table 3** provides a more comprehensive list to give a more complete perspective of the scope of the problem and some of its clinical implications.

DISCUSSION

Substandard and falsified medical products and medications are a global problem. The WHO estimates that up to 10% of medications worldwide are counterfeit; this figure may be 30% in parts of Africa, Asia, and Latin America.[19] Moreover, most online or Internet-based pharmacies are noncompliant with federal, state, or industry standards, and many countries lack a rigorously functioning pharmaceutical regulatory agency. Counterfeit medications generate an estimated $75 billion in annual revenue and cause up to 100,000 deaths worldwide each year.[20]

Scope of the Problem in Dermatology

Adverse events associated with counterfeit medications are inevitable. **Table 3** lists additional adverse dermatologic side effects, ranging from chemical burns, skin abscesses, alopecia, and fixed drug eruptions attributed to counterfeit pharmaceuticals.

The scope of counterfeit medications in dermatology also includes substandard, fraudulent, and unlicensed dermatologic drugs and treatments. For example, four patients in Florida developed botulism after cosmetic injections with unlicensed botulinum preparation.[21] The injections contained 3000 times the estimated fatal toxin dose. This example shows that unlicensed botulinum products can cause serious illness and highlights need for strict compliance with (or enforcement of) existing regulations.

Illicit or unregulated products can cause adverse health outcomes. Illicit cosmetic fillers have caused several deaths,[22] leading to an awareness campaign by the American Society of Plastic Surgeons.[22] Cases include a 35-year-old transsexual woman presenting to an emergency room with tachypnea, tachycardia, and cyanosis. The patient was in shock after receiving multiple subcutaneous gluteal injections of polymethyl methacrylate (PMMA) microspheres.[23] Because of the patient's history of PMMA injections 4 days earlier, along with the absence of infectious signs, such as fever or blood culture growth, the authors hypothesize that the PMMA induced the systemic inflammatory response syndrome. Another case details a 66-year-old woman who developed heart failure and an inflammatory reaction after illegal cosmetic injections of PMMA or polyacrylamide hydrogel.[24]

Mesotherapy is intended to improve one's overall appearance of health and to decrease signs of aging by promoting lipolysis through subcutaneous injections of preparations containing vitamins and natural plant extracts.[25] One form of mesotherapy is FDA-approved for decreasing submental fat but many others, often marketed as "biorejuvenation," are legal in parts of South America and Europe, but illegal in the United States. Mesotherapy can involve injection of various substances, ranging from off-label use of approved injectable medications to homemade "herbal" preparations including bile acids, caffeine, and plant extracts. Adverse effects of injection with unregulated substances range from noninfectious suppurative panniculitis[26] to cutaneous tuberculosis[27] and are well-reported in the literature.

Bacterial contamination of injected medications and diluents is another hazard of irregularly prepared products. Infection with atypical mycobacteria is a well-described consequence of improper injection practices or nonsterile diluents.[28] A niche but telling example: the presence of postinjection abscesses and granulomas in children adopted from orphanages in Russia and other former Soviet states.[29]

According to the adoptive parents, the orphanages want children adopted from their facilities to arrive in their new homes healthy, infection-free, and with robust appetites. Therefore, the children were injected with vitamins and prescription medications, allegedly antibiotics "to prevent infections" and possibly glucocorticoids "to increase the child's appetite when the family arrives at the new home." Oftentimes, children receive injections of vaccines, vitamins, and medications that may be unnecessary or administered with improper technique. The injected products may be prepared with nonsterile diluents, such as tap water, which often contain atypical mycobacteria living in the biofilm of the water taps. Indurated lesions at injection sites, often the upper-outer buttocks, of these children may represent infections, hematomas, reactions to vaccine adjuvants, and/or sterile abscesses.

Scope of the Problem Beyond Dermatology

Substandard and falsified medications appear in almost every area of medicine and have staggering effects on the health of individuals and populations. Particularly egregious examples include false vaccines, completely devoid of antigenic material, distributed in China[30]; counterfeit or substandard antimalarials in South East Asia[31,32];

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and contraceptive pills in Brazil that contain only starch and thus had no hormonal action.[33] These examples can have significant consequences, some of which are obvious (eg, unplanned pregnancies in the case of bogus oral contraceptives) and some less apparent (eg, vulnerability to vaccine-preventable diseases in the case of ersatz vaccines).

Manufacturers of counterfeit pharmaceuticals use sophisticated techniques to make their products nearly indistinguishable from authentic agents. A team investigating health-related crimes in Southeast Asia found that substandard artesunate, sold to treat malaria, was packaged in boxes with fraudulent holograms, designed to resemble proper packages of authentic artesunate.[32] Another report describes online-purchased counterfeit sildenafil arriving with individual capsules secure in seemingly genuine blister packets but packaged with falsified company logos and stamped with phony lot numbers.[34,35]

In many countries, national regulatory authorities permit over-the-counter sale of antibacterial and antimalarial agents. Frequent use, often without medical indication or in the wrong dose and duration, contributes to antimicrobial resistance. In India, several oral and parenteral antibiotics (eg, gentamicin, piperacillin-tazobactam, linezolid, and tigecycline) are approved for use but are not included in the national drug schedule and are therefore available without prescription.[36]

A Centers for Disease Control and Prevention study released in 2016 found that US-based dermatologists prescribe antibiotics at rates higher than any other specialty.[37] There is concern that dermatologists overprescribe antibiotics, especially when written for prophylaxis of perioperative infections.[38,39] Therefore, dermatologists may be unwitting contributors to widespread antibiotic resistance. This consequence is presumably more pronounced in countries where antibiotics are not tightly regulated and where fraudulent antibiotics are commonly sold.

Monitoring and detecting potentially fraudulent behaviors and practices is difficult, time-consuming, and costly. As a result, the world of fraudulent and counterfeit medications is unmonitored, which lowers the risk of intervention by law enforcement, making the enterprise especially attractive to organized crime.

The pharmaceutical supply chain is multistepped and complex. Many steps are vulnerable to corruption, from obtaining base materials; manufacturing the active ingredients; and storing, transporting, and distributing product. The expansion of Internet pharmacies further complicates the task of monitoring the distribution and sale of counterfeit medications.[19]

The production and sale of counterfeit, substandard, and missing medications is a profitable endeavor, especially when specific drugs are in short supply. Drug counterfeiters can take advantage of a high-demand market by charging exorbitant prices.[19] For example, during a brief period in 2011, drugs in short supply had price markups averaging 650% and soared up to 4533% for labetalol.[40]

Penalties for engaging in these activities are weak or nonexistent. The criminal penalties associated with illegally sale of narcotics are much higher than those associated with the sale of counterfeit drugs.[19]

Many organizations, governmental and nongovernmental, are taking steps to address the problems associated with SSFFC products (**Box 1**). In this regard the International Coalition of Medicines Regulatory Authorities provides “a global architecture to support enhanced communication, information sharing, crisis response and address regulatory science issues.”[43] The FDA and regulatory agencies for most European countries and developed nations worldwide are members of the International Coalition of Medicines Regulatory Authorities.

The International Police (Interpol) and the Medicines and Healthcare Products Regulatory Agency of the WHO manage a program called Operation Pangaea. This is an annual week-long event that addresses the online sale of counterfeit and illicit pharmaceuticals. Since its launch in 2008, participation in Operation Pangaea has grown from 10 countries to more than 100. The results include seizure of 21-million units of fake and illicit medicines, more than 150 arrests, launching more than 400 investigations, removing hundreds of Internet advertisements for illicit pharmaceuticals, and shutting down greater than 2400 Web sites.[44]

The United States has also taken legislative action. President Barack Obama signed the Drug Quality and Security Act into law in 2013, allowing secure tracing of medical products from manufacturer to pharmacy. This track-and-trace system makes it difficult for counterfeit drugs to enter the legitimate pharmaceutical supply chain.[19] Successfully combatting this problem requires continued collaboration among governments, law enforcement agencies, pharmaceutical industries, and the public.

Helping patients avoid adverse side effects from counterfeit medications also requires participation of providers in all medical fields. Providers are becoming more accustomed to asking patients about over-the-counter medications, herbal and

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Box 1
Steps to take with suspected substandard or falsified products

Reporting to the FDA[41]

To report a life-threatening situation caused by an FDA-regulated product online or in store, first call 911, then call 1-866-300-4374, the FDA emergency hotline.

As a consumer or health care professional, if you believe that you have a suspect counterfeit drug, report it to the FDA's MedWatch Office (www.fda.gov/Safety/MedWatch) and contact the pharmacy or company from where the drug was purchased.

If you suspect that a Web site is selling counterfeit drugs, report it to the FDA (www.fda.gov/Safety/ReportaProblem/ucm059315.htm). If you purchase drugs from an online pharmacy, make sure that it is one of the Verified Internet Pharmacy Practice Sites (VIPPS) accredited through the National Association of Boards of Pharmacy.

If you are aware of suspicious activities associated with counterfeit drugs, report it to the FDA's Office of Criminal Investigations (www.accessdata.fda.gov/scripts/email/oc/oci/contact.cfm).

Reporting to the WHO[42]

If you think a product you have used is a substandard or falsified product, report it to the WHO via their rapid report system. The WHO will investigate the claim, and if the threat is validated and poses a harm to public health, a Medical Product Rapid Alert will be issued (www.who.int/medicines/regulation/ssffc/medical-products/en/).

Reporting to Interpol

To contact Interpol to inquire about possible pharmaceutical crime, you may fill out an inquiry form from their Web site (www.interpol.int/Forms/Pharmaceutical_crime). This is not a tracking or reporting system. Reports should be directed to the FDA or WHO, agencies that then share collected information with Interpol to coordinate responses.

dietary supplements, and so forth. Providers should also ask patients about medications obtained abroad, received from family members abroad, or that may have been brought into the United States illegally ("unsupervised importation") and subsequently sold (eg, in ethnic markets and shops).

All physicians should be aware of problems associated with fraudulent medications; dermatologists must remember that fraudulent medications, just like authentic ones, can cause cutaneous adverse reactions. In general, when physicians evaluate a suspected drug eruption, their cognitive process starts by matching lesional morphology with the medication classes to which the patient has been exposed. This line of inquiry is difficult, however, when the culprit medication is an unidentified and unsuspected adulterant, contaminant, or substitution.

Counterfeit drugs comprise a growing percentage of the pharmaceutical market in the United States, and an even greater percentage in developing countries, many of which lack a well-functioning pharmaceutical regulatory agency.[19] Moreover, most online pharmacies are noncompliant with federal, state, or industry standards. Although this is a growing public health concern worldwide, consumers are largely unaware of the spectrum of consequences associated with fraudulent medications.

Fraudulent medications interfere with the treatment of individual medical concerns, with primary prevention of disease, with secondary containment of disease, with maintaining or improving health, with limiting the spread of drug-resistant pathogens, with potential overdosing or poisoning, with direct adverse reactions, and with drug-drug interactions. These consequences affect individuals, families, communities, and entire populations.

CLINICS CARE POINTS

- A thorough medication history will include questions about medications obtained abroad, received from family members abroad, brought into the United States as an "unsupervised importation", or that were obtained at internet pharmacies or ethnic markets and shops.
- Substandard medications can enter the supply chain at many points, eg, manufacture, packaging, importation, distribution, storage, dispensing, and sale.
- Do not use products, even cosmetic ones, that are imported illegally or possibly produced under fraudulent or substandard circumstances.
- Mechanisms to report possible substandard medications to the Food and Drug Administration are straightforward and an essential part of maintaining the health of individual paitients, their families, the local community, and the public at large.

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