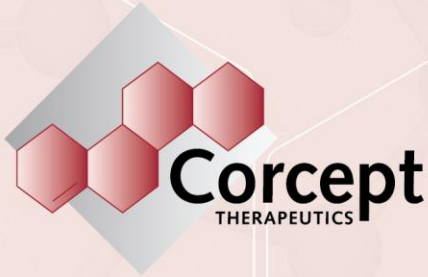

Drug Supply Chain Safety
Measures to combat Counterfeit Medicines.

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Ayse Baker BIO

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Ayse Baker has over 25 years' experience in pharmaceutical industry with focus on building and leading regulatory affairs teams worldwide. Ayse held increasing regulatory roles in both large and small pharmaceutical companies. Ayse started her career in pharmaceutical industry at Abbott Laboratories as a research scientist.

Ayse received a PhD in Chemistry from University of Illinois at Chicago. MBA from Lake Forest Graduate School of Management. She completed her post- doctoral fellowship at Loyola University Stritch School Medicine in Department of Hematology and Oncology. She was awarded Outstanding Young Investigator Award of Biochemistry /Biophysics Ayse is active and a frequent speaker in national and international trade organizations and prestigious academic institutions. She was recognized for her contributions to the Regulatory Affairs profession by the trade organization and became a Fellow of the Regulatory Affairs Professional Society (RAPS) in 2016 and currently serves on the RAPS Board of Directors.

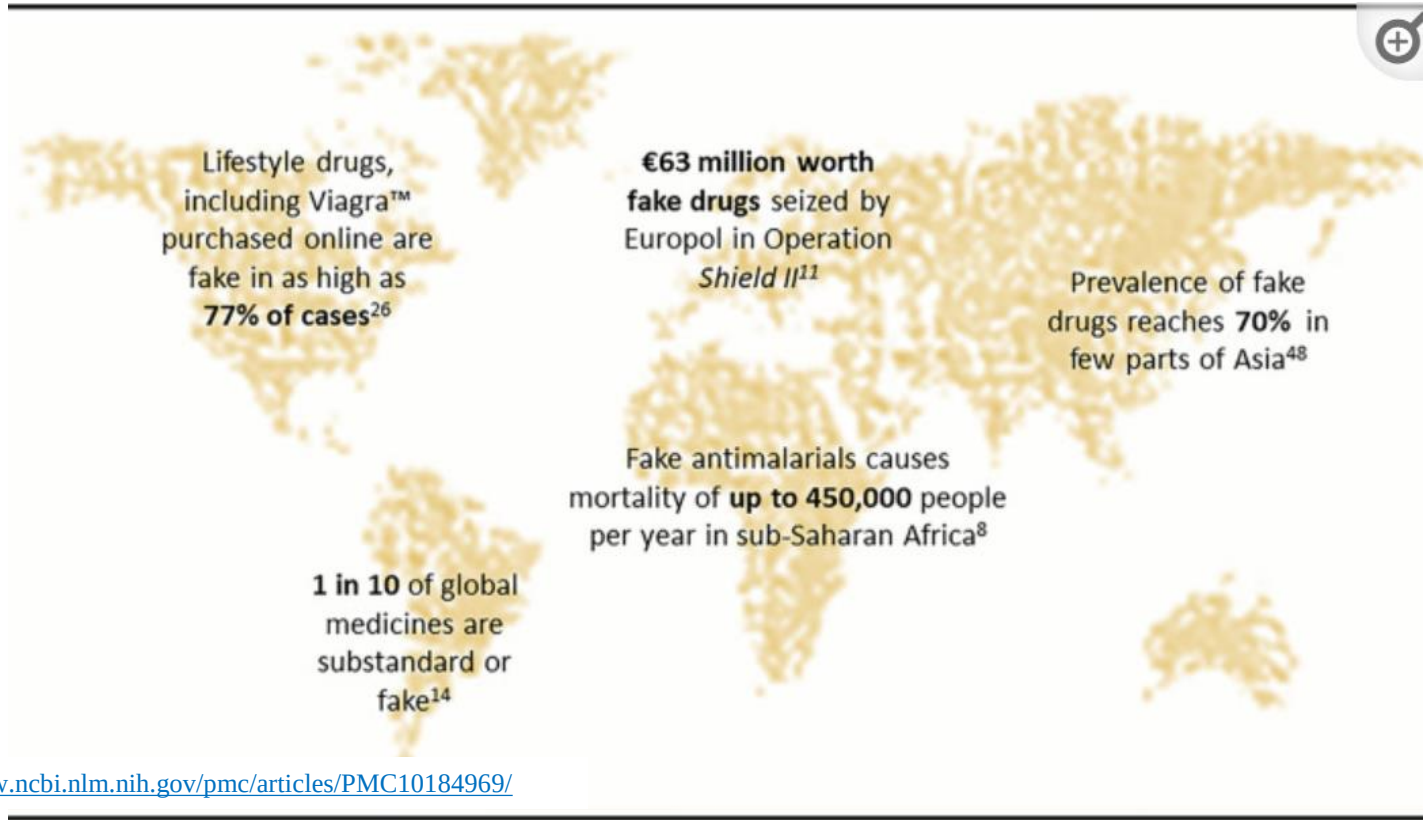
Counterfeit Medicines : A Global Problem

- Counterfeit medicine trafficking is one of the world's fastest-growing criminal enterprises
- Estimated global counterfeit market to be worth between US$200 and US$432 billion
- They are available via illegal street markets, websites, legitimate pharmacies, clinics, and hospitals

Source **https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9031510/**

Drug counterfeiting highlights across the globe

The whole world is dealing with the impact of a rise in counterfeit medicines



Source https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10184969/

Introduction

- The prevalence of counterfeit drugs is a problem. As the world's population grows, more people are suffering from different ailments and demand for drugs is increasing.
- Sick people tend to have an inelastic demand for drugs and medical devices.
- Counterfeiters are well aware of this and take advantage of the situation to traffic in fakes.
- The enormous market, and a huge profit margin creates opportunities for easy money that entice criminals to pursue the production of counterfeit drugs.
    - They cut corners in essential aspects of drug production and offer counterfeit products at significantly lower prices.

Background

Counterfeit medications are drugs that are deliberately and fraudulently mislabeled.

Their quality is unpredictable because they might be made with the correct formulations, or with the wrong formulations, or without the active ingredients, or with insufficient amounts of the active ingredients, or any combination of the aforementioned.

All counterfeit drugs are 100% illegal, whether they are “harmless” or not. It is a criminal offense to manufacture, process, pack, or otherwise distribute counterfeit pharmaceuticals or medical devices.

Defining Counterfeit Medicines

There is no universally accepted definition of counterfeit medicines. World Health Organization (WHO) uses labels like “substandard”, “falsely labelled”, “falsified”, and “counterfeit” to characterize medicines that are forged to seem genuine .

The term is not synonymous with low-cost generics. Generics is just as safe and effective as existing brand-name versions protected by intellectual property.

Counterfeits may contain

- no active ingredients, incorrect amounts, or incorrect ingredients (eg, chalk, mercury, paint, deadly poisons).
- significant impurities and contaminants, generic or branded, and claim to cure life-threatening conditions like cancer, or routine ones.

Source https://www.who.int/en/news-room/fact-sheets/detail/substandard-and-falsified-medical-products. 2018

"counterfeit drug" per 21 USC 312 -

(2) *The term "counterfeit drug" means a drug which, or the container or labeling of which, without authorization, bears the trademark, trade name, or other identifying mark, imprint, or device, or any likeness thereof, of a drug manufacturer, processor, packer, or distributor other than the person or persons who in fact manufactured, processed, packed, or distributed such drug and which thereby falsely purports or is represented to be the product of, or to have been packed or distributed by, such other drug manufacturer, processor, packer, or distributor.*

Generic Medicines vs. Counterfeit Medicines

It is important to establish that generic medications that offer original brand medications at a lower cost are not counterfeit or fake medications.

Generic medications undergo vigorous testing to ensure the quality of the medication is very close to equal to the original drug formulation and have the same effects on patients.

These medications must undergo quality control testing in order to be approved for public use and the labeling must be accurate, similar to the requirements for new drugs entering the market.

Source https://www.news-medical.net/health/Counterfeit-Medications.aspx

Issues with Counterfeit Medications

There are several different errors that may be intentional or accidental that may cause a medication to be classified as counterfeit. These include:

- Inappropriate dose of active ingredient
- Absence of active ingredient
- Altered absorption of the drug by the body
- Presence of additional ingredients
- Inaccurate or false packaging or labels

Public Health Implication

- Counterfeit medicine proliferation is a more significant public health threat than diseases they purport to cure.
- Those containing no active ingredients may be just as dangerous as those containing contaminants.
- At best, such medications do not treat the ailments they purport to treat.
- At worst, they contain toxic ingredients that outright kill patients.

Regulatory Perspective - FDA

Drug Supply Chain Security Act (DSCSA)

- FDA is implementing key provisions of the Drug Supply Chain Security Act (DSCSA), which outlines steps to achieve interoperable, electronic tracing of product at the package level to identify and trace certain prescription drugs as they are distributed in the U.S.

Actions & Enforcement

- All imported shipments of FDA-regulated products are electronically reviewed by the FDA.
- Imported drugs must meet FDA's standards for quality, safety and effectiveness. FDA verifies compliance with the following requirements as applicable: registration, listing, drug application, drug labeling and drug current good manufacturing practices (cGMPs).

Draft Guidance *Incorporation of PhysicalChemical Identifiers into Solid Oral Dosage Form Drug Products for Anticounterfeiting*

- for pharmaceutical manufacturers who want to use physical-chemical identifiers (PCIDs) in solid oral dosage forms (SODFs). A PCID is a substance or combination of substances possessing a unique physical or chemical property that unequivocally identifies and authenticates a drug product or dosage form.

Counterfeit Drugs and Online Pharmacy

- The problem of counterfeit medications is a rising issue with the introduction and growth of online pharmacies.
  - Online pharmacies offer a beneficial service for individuals to access medications, often at a lower price

- The medicines bought online through an online pharmacy are more likely to be counterfeit than those bought in a physical pharmacy.

- In developed markets, a growing number of counterfeit products are being sold through fraudulent online marketplaces.

FDA - Action & Enforcement

FDA's Office of Criminal Investigations conducts criminal investigations of illegal activities involving FDA-regulated products, arresting those responsible, and bringing them before the Department of Justice for prosecution. This includes cybercrime and distribution of counterfeit, unapproved, and misbranded medical products.

Three Darknet Fentanyl Vendors Sentenced to Over 20 Years in Prison

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Department of Justice
U.S. Attorney's Office
Eastern District of Virginia

FOR IMMEDIATE RELEASE
Friday, July 14, 2023

ALEXANDRIA, Va. – A Tempe, Arizona, woman was sentenced today to 5 years in prison for her role in operating multiple darknet pages selling illicit drugs alongside two previously sentenced co-conspirators.

FDA Consumer Information

Consumers may turn to online pharmacies because of convenience, privacy and cost savings, some websites sell medicines that are dangerous or even deadly

- Related to Consumer Information, below are the sites listed in FDA website

- BeSafeRx How to Buy Medicines Safely from an Online Pharmacy
- Flickr -- Counterfeit Drugs Photos
- Counterfeit Medicines: Filled with Empty Promises
- Counterfeit Alert Network

FDA Collaborations- U.S. Customs and Border Protection

FDA works with other agencies as well as private companies to secure the supply chain of medical products.

Partnership between the FDA and the U.S. Customs and Border Protection helps to track and intercept counterfeit drugs coming from overseas.

The FDA has also created industry standards as part of anti-counterfeiting initiatives, such as guidance about imprinting identifiers on pills

FDA Collaborations - USPTO

To combat the trafficking in counterfeit medicines, the USPTO

- tracks relevant domestic and international legislation
- works with foreign governments, law enforcement agencies, regulatory bodies, and IP offices to
  - (a) raise awareness about the dangers of counterfeit pharmaceuticals
  - (b) train inspectors, agents, regulatory, and legislative officers to better identify, seize, investigate, prosecute, and deter the consumption and sales of these illicit products.

Source : https://www.uspto.gov/ip-policy/enforcement-policy/counterfeit-medications

Response of the Pharmaceutical Industry

Counterfeit medications are a significant problem for pharmaceutical industries that profit from the sale of genuine medications.

As a result, pharmaceutical manufacturers and distributors have been investing into certain measures to reduce the impact of counterfeit medications.

This includes creating technologies to trace and authenticate medications as a way to reduce the impact and feasibility of counterfeit drugs.

Industry Perspective – Pfizer

Combating Counterfeits Through Technology and Partnersh

Pfizer aims to raise awareness & share experience of individuals affected by fake drugs.

Pfizer also combats the sale of counterfeit drugs by building anti-counterfeiting laboratories.

Pfizer's Global Security team partners with the law enforcement community to identify counterfeit medications and respond to reports of counterfeits.

Through these partnerships and using advanced lab equipment that helps determine drug authenticity, Pfizer has helped prevent over 302 million counterfeit doses from reaching patients since 2004.

Industry Perspective - Gilead

Foster City, Calif., January 19, 2022 – Gilead Sciences announced today that the company has taken action to protect the health and safety of the public from an expansive, criminal counterfeiting network responsible for distributing counterfeit and tampered Gilead HIV medication within the U.S. supply chain. As part of an ongoing investigation and litigation, in coordination with the U.S. Marshals and local law enforcement, Gilead has executed seizures at 17 locations in eight states, seizing thousands of bottles of Gilead-labeled medication with counterfeit supply chain documentation, including bottles labeled as the HIV medicines Biktarvy® (bictegravir 50 mg, emtricitabine 200 mg, and tenofovir alafenamide 25 mg tablets) and Descovy® (emtricitabine 200 mg and tenofovir alafenamide 25 mg tablets). Gilead continues to work closely with the U.S. Food and Drug Administration (FDA) and law enforcement to remove counterfeit and tampered medication from circulation and to prevent future distribution of counterfeit medications.

Industry Perspective - Gilead

Gilead's Position

At Gilead we are inspired by the opportunity to address unmet medical needs for patients living with life-threatening diseases around the world. The nature of Gilead's products makes ensuring authenticity and safety of our medicines fundamentally important.

Gilead's Anti-Counterfeiting Team consists of brand protection, legal, security, supply chain, quality, and packaging professionals who collaborate to address the threat to patient safety associated with counterfeiting and diversion of Gilead medicines. Gilead's Anti-Counterfeiting Team uses measures to detect, stop, deter, and report illicit sales of counterfeit medicines.

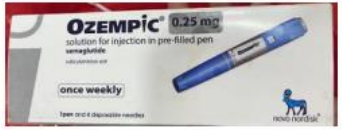
Industry Perspective - Novo Nordisk

Novo Nordisk warns of counterfeit Ozempic® (semaglutide injection) pen found in US

PLAINSBORO, N.J., June 16, 2023 – Novo Nordisk is working with the US Food and Drug Administration (FDA) and is alerting the public that a counterfeit Ozempic® (semaglutide injection) pen was found in the US.

The product was reportedly purchased at a retail pharmacy and the company is actively investigating the report and collaborating with the FDA to identify the origin and distribution of the counterfeit pen. The counterfeit product appears to have contained another type of diabetes medication, insulin glargine injection, that works differently than Ozempic®, which reportedly led to an adverse reaction

FDA approved Ozempic® pen in the US and counterfeit product

Authentic Ozempic® Pens	Counterfeit Product
With Cap  Without Cap  	With Cap  Without Cap 
Authentic Ozempic® Carton	**Counterfeit Carton**
 	

The Challenge

Counterfeit medicines are an enormous global health challenge

- The statistics look bleak, and it may seem impossible to change the forecast. But by creating barriers and focusing on innovation, pharmaceutical companies stand a chance of reducing those figures and protecting themselves and their consumers from counterfeit drugs.

- Lack of rigorous and universal drug regulations, the complex nature of the global pharmaceuticals supply chains, and the sophistication of counterfeit medicine packaging are among the factors that make it difficult for regulators, pharmaceutical firms, activists, and consumers to curtail the problem

Potential Solutions

Source https://blog.tracktracerx.com/5-strategies-to-combat-and-reduce-counterfeit-drugs-in-the-supply-chain#:~:text=Raise%20Awareness%20and%20Work%20with%20regulatory%20agencies.&text=The%20FDA%20also%20has%20a,and%20professionals%20in%20the%20area.

Solutions : Packaging

Packaging

- Add certain design elements to your packaging to make counterfeiting more difficult.

- Serialization on packaging is not only becoming an FDA requirement but also helps prevent counterfeit drugs from entering the supply chain.

Solutions – Awareness & Collaboration

Awareness and Working with Regulatory Agencies.

- Agencies such as the Food and Drug Administration (FDA) in the U.S., and the World Health Organisation (WHO) need participating pharma companies and countries to collaborate, raise issues and improve initiatives; such as stricter enforcement regimes for culprits and the latest guidelines and developments for companies to follow in line with prevention efforts.
- The FDA also has a counterfeit alert network which notifies members of their network if counterfeit medicine has been reported.

Solutions – Supply Chain Security & Integrity

Supply Chain Security

- Dedicated supply chain security is important and might be worth investing in a dedicated security body that are specialized in the field.

Supply Chain Security Integrity & Verification Points

- verification points at different links in the chain
- Some key links in the chain are where raw materials are received at a facility, after these are processed; dosed into vials for example, as well as when units are packed into cartons and pallets and also when these are received at distribution centres.

Solutions – Traceability

Traceability – Most important

- robust, user-friendly, seamless and secure traceability system.
- a traceability system is a solid foundation for effective execution

Traceability allows pharma companies to respond quickly by

- Acting quickly with product transparency
- Identifying the scope of the problem
- Locating the counterfeit drugs quickly
- Locating affected lots and impacted locations/customers
- Initiating recall of the product with the surrounding recall logistics

Conclusion

- Counterfeit pharmaceutical products are a global issue with a significant financial impact .
- More worryingly, poses potential dangers to patients' health.

Active collaboration between nations, pharmaceutical companies and regulatory bodies is essential to formulate a cohesive plan to effectively prevent drug counterfeiting.

THANK YOU !

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- https://www.pharmtech.com/view/blocking-the-threat-of-counterfeit-medicines

DSCSA - The Drug Supply Chain Security Act (DSCSA)

The Drug Supply Chain Security Act (DSCSA) was passed in November 2013. It is intended to provide guidance to the FDA on new standards for drug distribution in the United States, making it easier to detect and remove potentially dangerous drugs from the pharmaceutical supply chain.

This law requires that there is traceability and reporting of product licensing from end to end within the supply chain, ensuring the safety of the end consumer.

Through an electronic communication model, the participants in the chain exchange important data with the responsible body (.XML standard), which makes the management of the movement and commercialization of medicines and prescription drugs in the country more efficient.

DSCSA: legislation and requirements

The legislation and requirements on serialization and traceability of medicines ensure the safety of pharmaceutical products, **combating theft, drug diverting and counterfeiting**.

These requirements also **facilitate recalls** and **saleable returns** within the supply chain, reducing costs and negative impacts on the business.

Furthermore, by having that visibility of information, the origin of the medicines can be ascertained.

This directly impacts the **safety of the end consumer** and the reputation of the distributors participating in the chain.

DSCSA: serialization and pharmaceutical packaging

The first step to efficient drug traceability is the implementation of serialization.

Serialization assigns a unique bar code, called a **single code**, to each medicine package, and it must be imprinted.

The structure of this code is defined by specific US regulations, in line with GS1 standards.

DSCSA-Compliant Systems 12-Month Stabilization Period

FDA Reiterates November 2023 Deadline for DSCSA-Compliant Systems with 12-Month Stabilization Period

FDA guides industry not to slow or delay projects and use 12-month period to stabilize systems

DSCSA-Compliant Systems 12-Month Stabilization Period

- On August 25, 2023, the U.S. Food and Drug Administration (FDA) released a “Guidance for Industry” document related to the Enhanced Drug Distribution Security (EDDS) provisions of the U.S. Drug Supply

- Chain Security Act (DSCSA) that goes into effect on November 27, 2023.The FDA has heard from stakeholders across the drug supply chain that trading partners need more time to stabilize systems that are regulated under the EDDS provisions.

- To ensure that products continue to move smoothly through the supply chain, the FDA has announced a 12-month stabilization period that extends through November 27, 2024, to give trading partners the time they need to finalize the implementation of DSCSA-compliant processes and systems.

- The FDA’s new guidance applies to all EDDS requirements for all trading partners, but the FDA reiterated that this is not a delay in the law and trading partners need to use this time to stabilize systems and processes.

DSCSA - Key Take Aways

- The FDA is urging trade partners to view the extra 12 months as a “stabilization period” to finish implementation, troubleshoot problems, and otherwise prepare their systems for accurate, secure, electronic data exchange

- The FDA reiterates that this guidance should not be used as a justification for trade partners to postpone implementation efforts. The law has not been delayed and the FDA can still penalize companies that violate it.

- The FDA announcement eliminates any ambiguity related to the deadline. The 12-month stabilization period applies to all segments: pharmaceutical manufacturers, wholesale distributors, and dispensers.