

HIMSS¹⁹ CHAMPIONS OF HEALTH UNITE

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Counterfeit Pharmaceuticals Supply Chain

Session 168 February 13, 2019

MITRE

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Agenda

- Learning Objectives
- The global problem of counterfeit and “fake” pharmaceuticals and medical devices
- The intersection of cost, quality and outcomes in the supply chain
- Program integrity best practices
- Supply chain replicable strategies to address



Learning Objectives

- Discuss the worldwide problem of counterfeit and fake pharmaceuticals and medical devices
- Identify strategies that address the intersection of cost, quality and outcomes in the pharmaceutical supply chain
- Integrate best practices of supply chain strategies that address the use of data analytics
- Discuss the construction and streamlining of supplier relationships to promote risk sharing

Counterfeit Medicines

- Counterfeit medicines are a significant threat to public safety
 - The number of detected counterfeit incidents are increasing
 - Counterfeiters are able to produce visually indistinguishable copies of branded products
 - Increase in counterfeiting of life-saving and sterile products increases public safety risks
- Counterfeit medicines are a global public health risk
 - Failure to receive intended therapeutic benefit
 - Medical harm from toxic materials contained within counterfeit formulations
 - Adverse reactions from non-sterile injections of counterfeit medicines
 - Development of therapy-resistant strains due to substandard counterfeit medicines



US Approach to Combatting Counterfeits

Drug Quality and Security Act (November 27, 2013)

Title I

- This law amended the Federal Food, Drug and Cosmetic Act to grant the Food and Drug Administration more authority to regulate and monitor the manufacturing of compounded drugs



Approach to Combatting Pharmaceutical Counterfeits in the United States

Title II: Drug Supply Chain Security Act (DSCSA)

<https://www.fda.gov/Drugs/DrugSafety/DrugIntegrityandSupplyChainSecurity/DrugSupplyChainSecurityAct/>

- Created requirements to facilitate the tracing of prescription drug products through the pharmaceutical supply distribution chain
- Focuses on change of ownership rather than change of possession
- Creates a transaction history that acts as title to the product
- Requirements for reporting suspect or illegitimate product
- Ultimately will create a databank for package level traceability



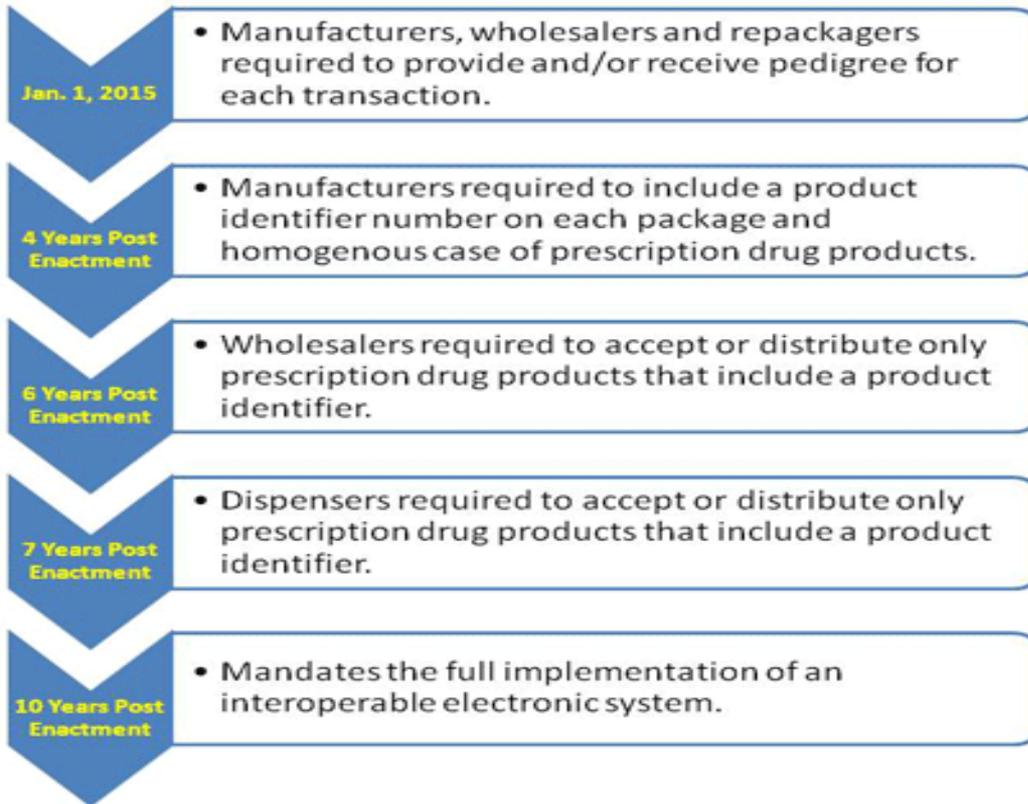
Approach to Combatting Pharmaceutical Counterfeits in the United States

Title II: Drug Supply Chain Security Act (DSCSA)

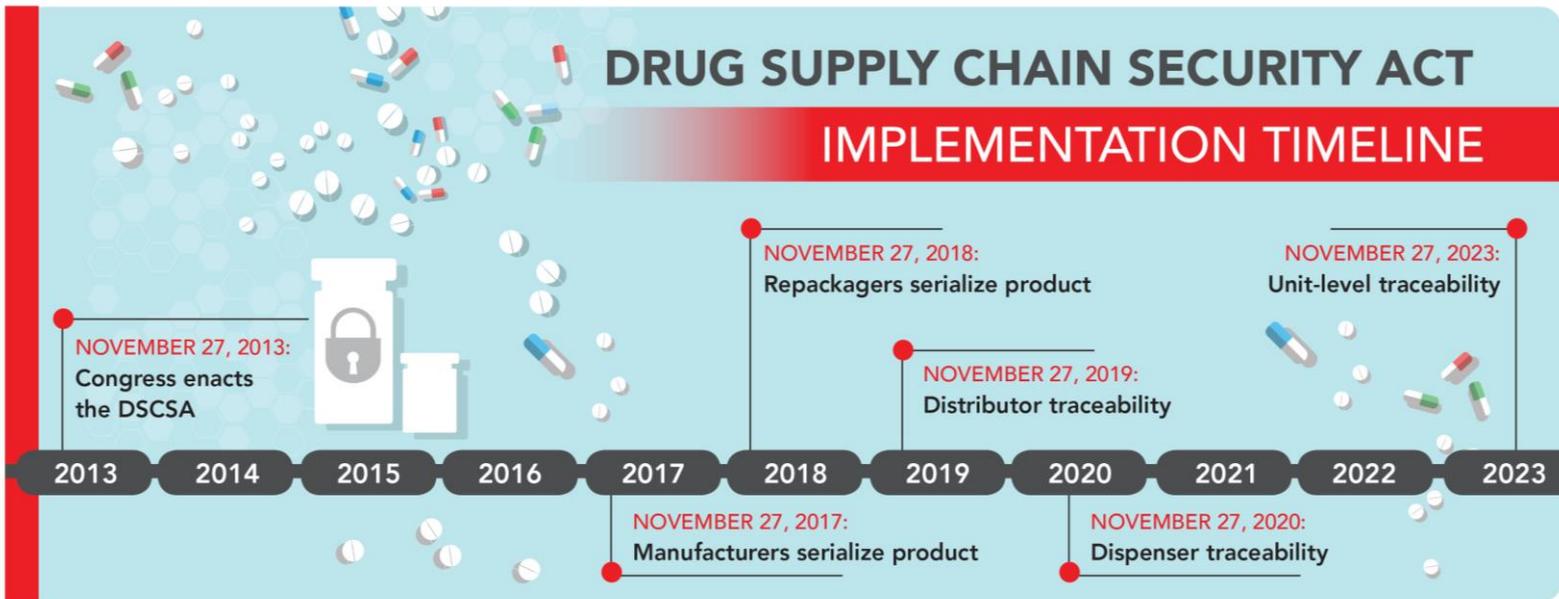
- Creates traceability from point of manufacture to dispenser
- Uses both 2D barcode and standardized numerical identifier
- Focuses on change of ownership rather than change of possession
- Creates a transaction history that acts as title to the product
- Requirements for reporting suspect or illegitimate product
- Ultimately will create a databank for package level traceability



DSCSA Timeline

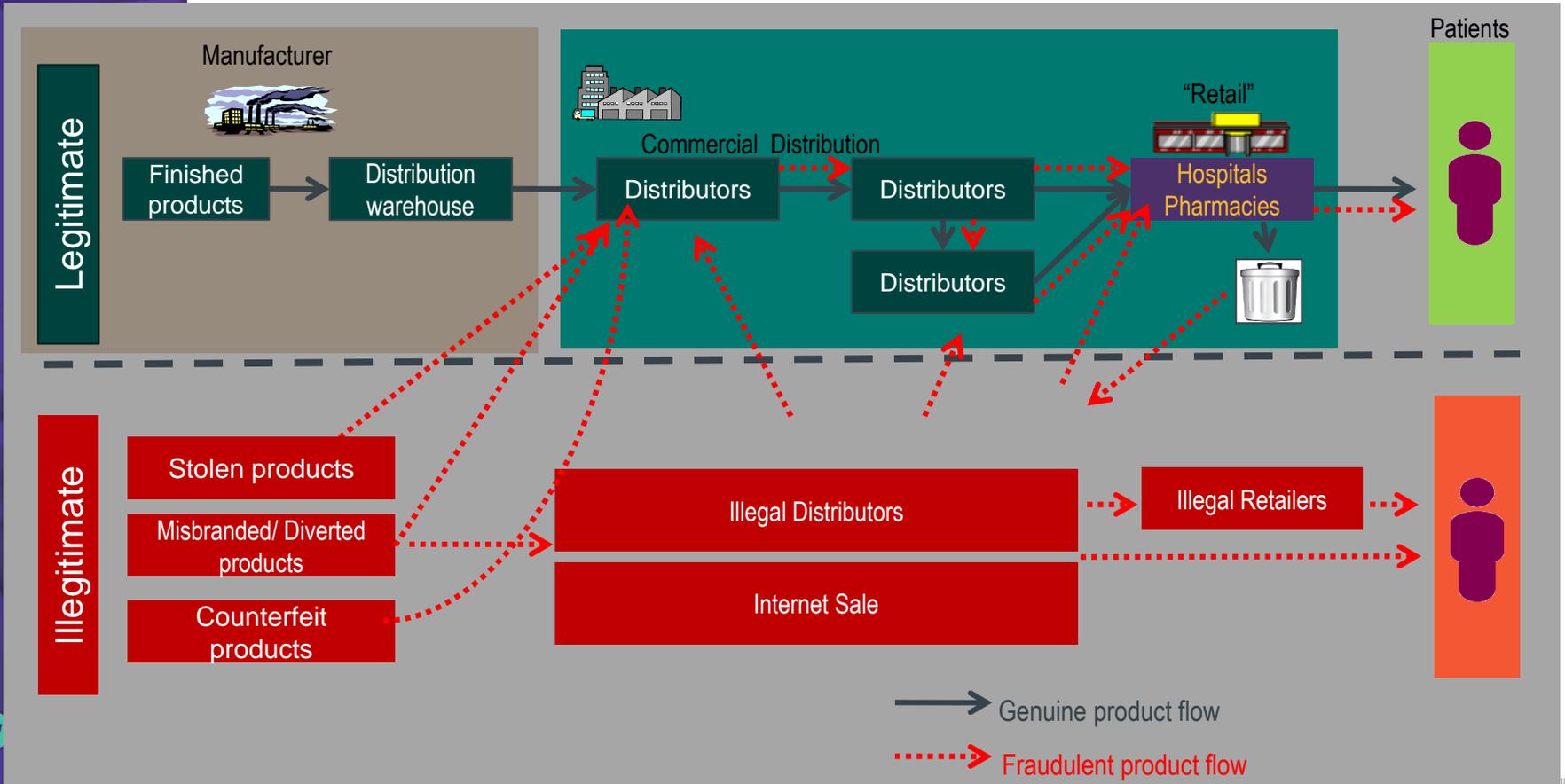


DSCSA Timeline

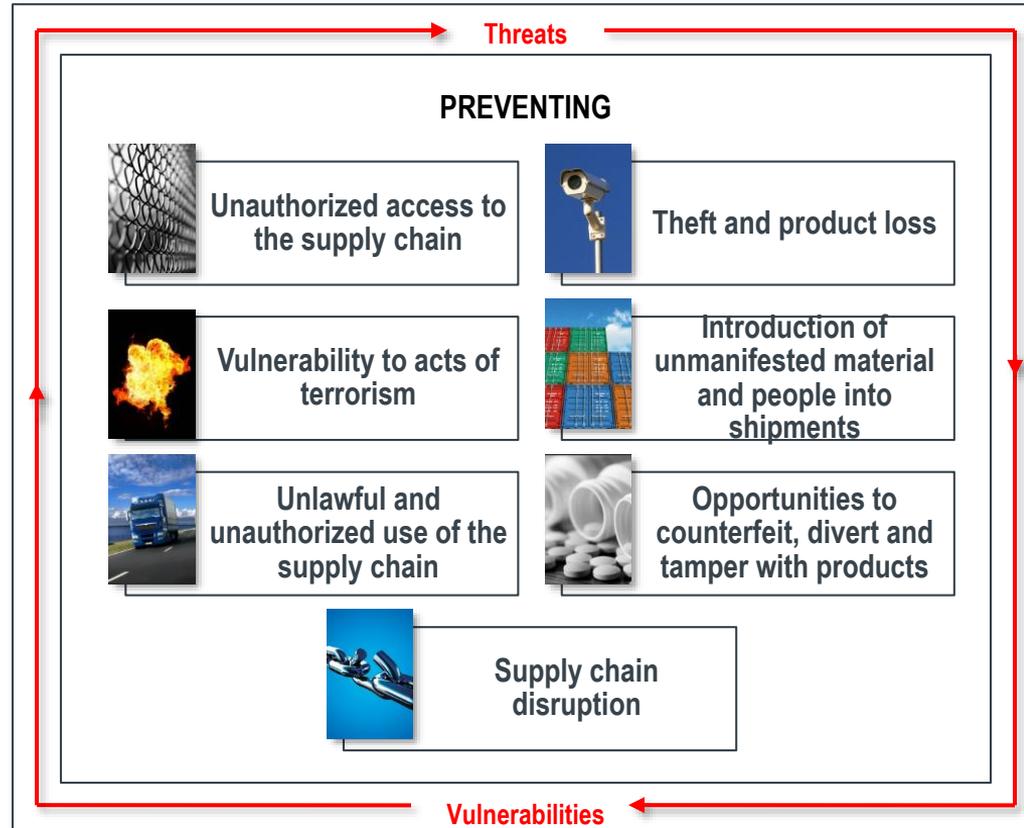


Source: <https://www.rdmag.com/article/2017/05/contract-manufacturers-juggle-serialization-demands>
 Andy Szal, Advantage Business Media's Manufacturing Group

Pharmaceutical Supply Chain



Supply Chain Security



Supply Chain Security

Security Risk Management

- Risk Assessment
- Subject Matter Expert Support
- Regulatory & Trade Security Compliance
- CAPA
- Industry Best Practices
- Security Audit
- Incident Management & Investigative Support

Policy & Procedures

- Minimum Security Standards
- Global Policy
- Procurement Contract Language
- SOP Development Support
- Resource Guides/FAQ

Engagement & Awareness

- Training Development
- Stakeholder Outreach
- Technology Assessment
- Industry Intelligence Awareness



Product Integrity Trends

Rogue online drug sellers

Reuse of authentic packaging components

Reverse distribution compromise

Cargo Theft

Drugs of abuse / illicit value

Humanitarian/Charitable/Discounted Goods
Fraud

Direct—to-physician marketing and distribution

Regulatory weaknesses

Organized criminal networks

Illegal generics of high value products

Drugs with limited access / availability

Counterfeit/diverted Biologics



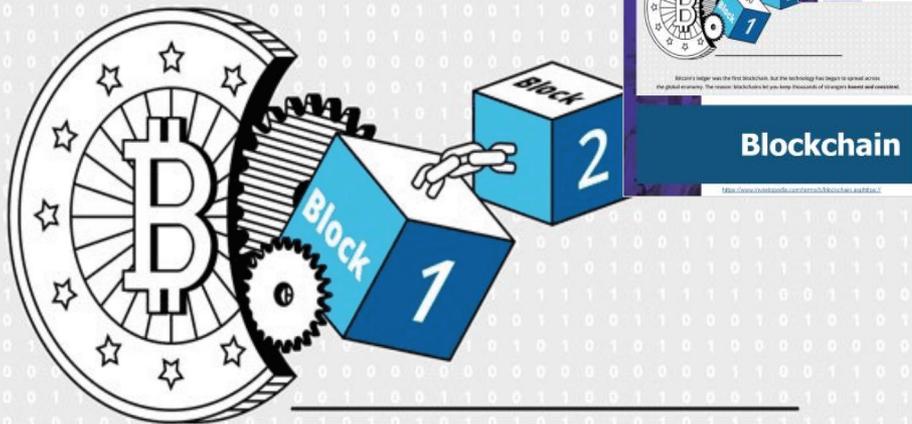
Blockchain (McKinsey and Company)*

Five common blockchain myths create misconceptions about the advantages and limitations of the technology.

	Myth	Reality
1	 <p>Blockchain is Bitcoin</p>	<ul style="list-style-type: none"> Bitcoin is just one cryptocurrency application of blockchain Blockchain technology can be used and configured for many other applications
2	 <p>Blockchain is better than traditional databases</p>	<ul style="list-style-type: none"> Blockchain's advantages come with significant technical trade-offs that mean traditional databases often still perform better Blockchain is particularly valuable in low-trust environments where participants can't trade directly or lack an intermediary
3	 <p>Blockchain is immutable or tamper-proof</p>	<ul style="list-style-type: none"> Blockchain data structure is append only, so data can't be removed Blockchain could be tampered with if >50% of the network-computing power is controlled and all previous transactions are rewritten—which is largely impractical
4	 <p>Blockchain is 100% secure</p>	<ul style="list-style-type: none"> Blockchain uses immutable data structures, such as protected cryptography Overall blockchain system security depends on the adjacent applications—which have been attacked and breached
5	 <p>Blockchain is a "truth machine"</p>	<ul style="list-style-type: none"> Blockchain can verify all transactions and data entirely contained on and native to blockchain (eg, Bitcoin) Blockchain cannot assess whether an external input is accurate or "truthful"—this applies to all off-chain assets and data digitally represented on blockchain

*<https://www.mckinsey.com/business-functions/digital-mckinsey/our-insights/blockchain-beyond-the-hype-what-is-the-strategic-business-value>.

Bitcoin is based on a *distributed* ledger, or rather a specific kind of distributed ledger



Bitcoin's ledger was the first blockchain, but the technology has begun to spread across the global economy. The reason: blockchains let you keep thousands of strangers *honest and consistent*.

Blockchain

According to McKinsey, "Blockchain is a distributed ledger, or database, which may be shared across a public or private computing network"

- "Each computer node in the network holds a copy of the ledger, so there is no single point of failure".
- "Every piece of information is mathematically encrypted and added as a new "block" to the chain of historical records".
- "Various consensus protocols are used to validate a new block with other participants before it can be added to the chain"
- <https://www.mckinsey.com/business-functions/digital-mckinsey/our-insights/blockchain-beyond-the-hype-what-is-the-strategic-business-value>.

Product Integrity Mission

Protect our Patients and Company Reputation

Protect Merck/MSD products from external illicit actions

- Counterfeiting
- Diversion
- Tampering/Adulteration
- Theft

Reactively respond to all Product Integrity complaints and indications

Proactively identify, assess, and mitigate Product Integrity threats to patients and Company

- Focus on intelligence-driven actions and outcomes
- Threat assessment → High-value target identification → Target interdiction

Enable meaningful enforcement actions

- Criminal
- Civil
- Administrative

Enable effective product security and supply chain security features and methodologies

Enable meaningful advocacy and awareness to patients and other key stakeholders

Innovate to create additional capacity and/or capability



Product Integrity Strategy

Protect our Patients and Company Reputation

Secure the Supply Chain

- Provide Supply Chain Security capacity that **maintains the security and integrity of Merck materials and products**
- Deploy the use of anti-counterfeiting **security features** to prevent counterfeiting and tampering, and enable **rapid authentication of questioned materials**

Investigations and Enforcement

- Provide **intelligence-driven proactive and reactive investigative capacity** engaging high-risk/high-value targets
- Provide robust **forensic analysis** capability to identify and characterize illicit products
- Enable **meaningful enforcement actions** that mitigate identified/confirmed threats

Raise public and stakeholder awareness

- Create public awareness campaigns and other communication tools to **effectively raise public awareness of threats to public safety** associated with illicit pharmaceutical products
- **Advocate for policy and regulatory changes** that further protect patient safety from these threats
- Provide industry thought leadership and collaboration to issues of illicit medicines

Use Data and Intelligence to meaningfully advance operational activities



What We Are Learning

- Recognize and appreciate the significance of the threat
- Don't underestimate the capabilities and applied effort of the counterfeiter
 - Highly motivated
 - Will do anything to make money
 - Everything can be copied
 - There are no rules
- Matter of supply and demand
 - Can artificially create demand
 - Need to create awareness of the supply
 - Someone will buy it
- Threat is constantly evolving
 - What happened yesterday not necessarily what is going to happen tomorrow
 - But we can be constantly learning and applying what we've learned



What We Are Doing

- Think like the bad guy
 - What do we know about their capabilities/limitations?
 - What are the vulnerabilities in our systems that can be exploited?
 - What is the next supply/demand issue that creates opportunity for counterfeiters?
- Develop effective threat detection capabilities
 - Identify triggers/indicators and monitor for them
 - Apply what we've learned to predict additional threats
- Develop effective threat mitigation capabilities
 - Product security features: development and application
- Develop effective enforcement strategies
 - Collaborative relationships with LE to support criminal actions
 - Civil enforcements
 - Administrative enforcements
- Mitigating external factors of Product Integrity risks



Targeted Products



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EU Regulators Warn of Counterfeit Copies of Cancer Drug Herceptin

Posted 16 April 2014
By Alexander Gaffney, RAC

EU regulators have issued a warning that several batches of the cancer medicine Herceptin (trastuzumab) have been "tampered with," falsified and reintroduced into the supply chain, potentially putting patients at risk.

Drug safety in oncology 3



Oncology drugs in the crosshairs of pharmaceutical crime

Bastian J Venhuis, Angela E Oostlander, Domenico Di Giorgio, Ruth Mesimann, Ines du Plessis

Oncology drugs clearly have become a target for pharmaceutical crime. In 2016, falsified oncology drugs ranked fifth in the most commonly falsified drug category among the reports received by the Pharmaceutical Security Institute. Although the prevalence of illicit oncology drugs in the legal supply chains appears to be small, these drugs are difficult to detect, particularly in clinical practice. Forthcoming countermeasures to detect illicit drugs in high-income countries include compulsory anti-tampering devices and product verification technology for a risk-based selection of medicines. Health-care professionals must implement these new procedures into their workflow and remain vigilant about those medicines that are not selected. Although countermeasures should firmly tighten supply chain security, there are concerns about how quickly pharmaceutical crime will adapt to these protections. Because patients and health-care professionals have shown a lenient attitude towards purchasing medicines from unreliable sources, measures against the highly accessible illegal medicine supply chain remain necessary. To improve detectability in clinical practice, *monitoring of inefficiencies and removal drug effects or adverse events or adverse drug reactions is essential.*

Lancet Oncol 2018; 19: e209-17
This is the third in a Series of three papers about drug safety in oncology

National Institute for Public Health and the Environment, Bilthoven, Netherlands
(A E Oostlander PhD,
B J Venhuis PhD), Italian Medicines Agency, Rome, Italy
(D Di Giorgio PhD), Illegal Medicines Control, Swissmedic,



AP February 7, 2013, 4:06 PM

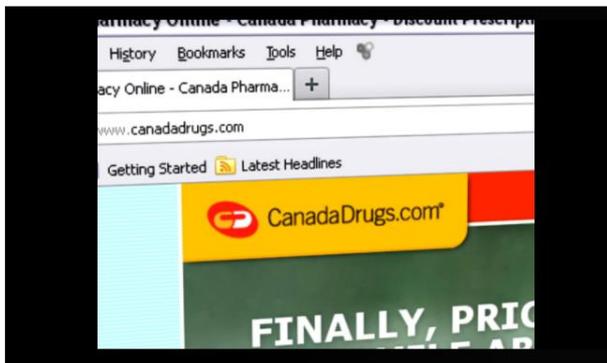
FDA warns about fake Avastin again



The FDA issued a warning on a popular cancer drug that turned out to be fake. The vials labeled "Avastin," contained a liquid that was worthless. But who would sell a fake to cancer patients? Chief investigative correspondent Armen Keteyian reports.

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WASHINGTON The Food and Drug Administration is warning doctors about another counterfeit version of the cancer drug Avastin distributed in the U.S., the third case involving the best-selling Roche drug in the past year.



By ARMEN KETAYIAN CBS NEWS March 22, 2012, 1:13 PM

Fake Avastin shipper tied to Canadadrugs.com

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(CBS News) - CanadaDrugs.com bills itself as the "largest and most trusted" online Canadian pharmacy. Based in an office building in Winnipeg, Manitoba, it says it

More fake Avastin found, this time in Cyprus



Five years after falsified versions of Roche's cancer drug Avastin first hit the headlines, fake packs are still being discovered in the supply chain.

Cyprus' Ministry of Health has revealed that three batches of fake Avastin – bearing the Altuzan tradename used in Turkey – have been identified on the northern (Turkish-speaking) side of the island. Avastin (bevacizumab) is used to treat a range of cancers, including colorectal, breast and lung cancer.



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Falsified Humira found in Germany

A parallel importer has discovered counterfeits of AbbVie's blockbuster Humira in the German supply chain.



The fakes of Humira (adalimumab) - the world's biggest-selling drug with turnover of \$11bn last year from use in rheumatoid arthritis, psoriasis and several other indications - seem to originate in Poland and Turkey and bear a falsified batch number that has never been used by AbbVie.

Phil Taylor

06-May-2015

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Abraxane Aclasta Actemra Alimta Aloxi Altuzan
Anzemet Aredia Artzal Avastin Boniva Botox
Doxil Dysport Eloxatin Erbitux Euflexxa Faslodex
ar H Merclon Hyalgan
cort Juvederm
Ultra 4
Mabthera
Menopur M
Mirena Neula
Perlane Perlane-L Pro
Radiesse Remicade Restylane-L Ristova Rituxan
Sandostatin-Lar Sculptra Supartz Synvise Synvise
One Taxotere Triamcinalone Velcade Venofer
Vidaza Xeomin Xolair Zometa

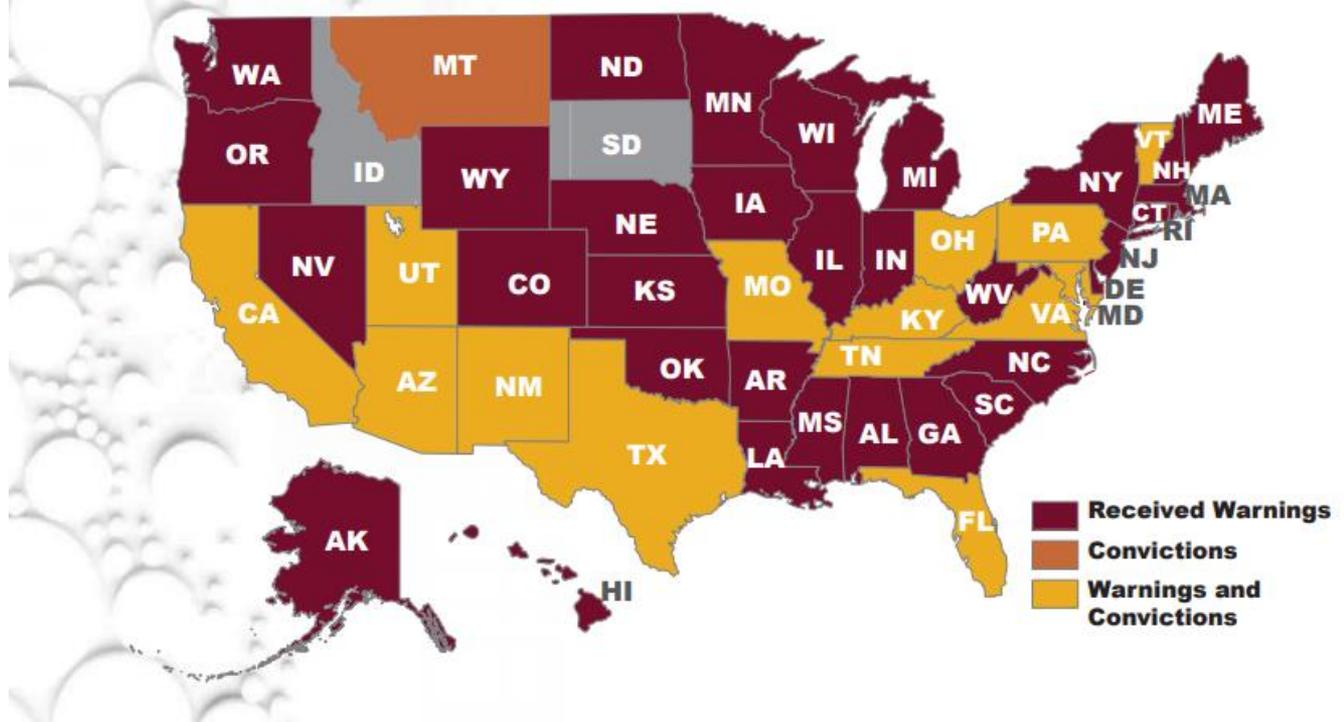


Every state in the U.S.

has had a counterfeit drug
incident since 2000



DOCTORS WARNED ABOUT FAKE CANCER DRUGS



Social Media/Cyber Threats



MITRE Proposal for Counterfeit Analysis

- Identify diversion/insertion points
- Follow the Active Pharmaceutical Ingredients (API)
- Import/Export records
- Identify illicit supply chains
- Comparison to other fraud or criminal activities
- Harness social media information
- Develop profiles, detect patterns, identify hot spots
- Create model that anticipates movement
- Consider/execute Blockchain to include the tracking of Opioids, Cold-Chain Pharmaceuticals and (API)



The Network's Analytic Cell Strategy

Using the Depth of MITRE and their partners

Analytic
Cells



Pharmaceuticals

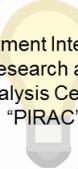


Medical Devices



Network Integrity

MITRE
Innovation



Payment Integrity
Research and
Analysis Center
"PIRAC"



Financial Crime
Analytics



National /
International
Intelligence



Social Media
"Hawkeye"



Supply Chains



Border / Port Security



Questions

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Please complete evaluation

