Counterfeit PDE5 Inhibitors Pose Significant Safety Concerns

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Disclosures

Consultant/Advisory Board Member

Allergan
Anteres
Auxilium
American Medical Systems
Coloplast Endo
Lilly
Neri / Ixchelsis
NIH
Therologix
Absorbent
Total Number of PDE5 I Prescriptions (1998 - 2003)

Source: US, IMS Health NPA Plus™

PDE5 Inhibitor Prescriptions per Year

Year
1998 1999 2000 2001 2002 2003

Total Prescriptions (Millions)
0 2 4 6 8 10 12 14 16 18
Total Rx Market Growth

Source: Verispan VONA
Contraction of PDE 5 inhibitor Market

- 6% decrease in PDE 5 i prescriptions in 2004-5
- Was honeymoon period for oral ED meds over?
- What was big pharma going to do about this?
- Multiple explanations for this observation
Contraction of PDE5 i market: Reasons

- Epidemiologic studies - MMAS, NHSLS, etc.
  - data over-estimated number of afflicted men & Rx seekers
- Cost - single pill relatively expensive
- Insurance – removal of Medicaid & HMO coverage
- Safety – cardiac concerns, hypotension, NAION, etc.
- Decreased interest in female estrogen supplements
  - diminished desire may reduce demand for male ED drugs
- Counterfeit PDE 5 i market – new phenomenon!
Counterfeit Pharmaceuticals

- Scope of the Problem
- Online/Internet Sales
- Patient Risks
- Addressing the Problem
Some Facts.....

• The WHO estimates 6-10% of products in the worldwide pharmaceutical market are counterfeit

• In poor countries, as much as 50% of available drugs are counterfeit or sub-standard

• Thousands of deaths globally (Cambodia, Haiti, Nigeria, etc) have been attributed to “fake” medications used to treat malaria, meningitis, etc

Source: WHO
## Examples of Counterfeit Drugs

<table>
<thead>
<tr>
<th>Country and Year</th>
<th>Counterfeiting Problem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nigeria, 1990</td>
<td>Cough mixture was diluted with a poisonous solvent leading to the deaths of 100 children.</td>
</tr>
<tr>
<td>Mexico, 1991</td>
<td>Anti-burn ointment contained sawdust.</td>
</tr>
<tr>
<td>Turkey, 1993</td>
<td>A pharmacist is arrested after the active ingredient in ‘drugs’ exported to Africa found to be baking soda.</td>
</tr>
<tr>
<td>Niger, 1995</td>
<td>A meningitis drug contained only water.</td>
</tr>
<tr>
<td>Haiti, 1996</td>
<td>59 children die after taking a counterfeit syrup for fever.</td>
</tr>
<tr>
<td>Kenya, 1998</td>
<td>Anti-malarial drugs were found to be ineffective.</td>
</tr>
<tr>
<td>India, 1998</td>
<td>Diethylene glycol poisoning killed at least 30 children.</td>
</tr>
<tr>
<td>Brazil, 1998</td>
<td>Ineffective contraceptive pills resulted in unwanted pregnancies.</td>
</tr>
<tr>
<td>Malawi, 1999</td>
<td><em>Africa Health Journal</em> reports an influx of counterfeit drugs into the country.</td>
</tr>
<tr>
<td>Italy, 2000</td>
<td>240,000 packs of medicines and 2t of raw materials seized.</td>
</tr>
<tr>
<td>China, 2001</td>
<td>The <em>Shenzhen Evening News</em> reports that more than 100,000 people died of fake drugs in 2001.</td>
</tr>
<tr>
<td>USA, 2001</td>
<td>Counterfeit <em>Serostim</em>, <em>Neupogen</em> and <em>Nutrupin AQ</em> discovered.</td>
</tr>
<tr>
<td>India, 2001</td>
<td>Police found 660 kg of fake drugs, 1000 kg of raw materials and boxes bearing the logo of a reputable firm. All of these were discovered in one factory.</td>
</tr>
<tr>
<td>Nigeria, 2002</td>
<td>The head of the country’s drug control agency reported that 60% of the drugs were counterfeit, substandard, or expired.</td>
</tr>
<tr>
<td>USA, 2002</td>
<td>The FDA reported 3 lots of counterfeit Combivir.</td>
</tr>
<tr>
<td>China, 2002</td>
<td>Counterfeit drugs valued at USD 57 million were identified.</td>
</tr>
<tr>
<td>USA, 2003</td>
<td>Recall of 200,000 bottles of the anti-cholesterol drug, <em>Lipitor®</em>.</td>
</tr>
</tbody>
</table>

*Analyst, 2005, 130, 271-279.*
A Growing U.S. Problem

• U.S. government estimates that counterfeiting costs the American economy $200 billion annually

• Counterfeit drug sales $39 billion in 2005 and went up to $75 billion in 2010

• **Equals 14% of legitimate pharmaceutical sales**
  – 13% annual growth rate vs 7.5 percent annual growth for global pharmaceutical commerce

• Shift from “mom and pop” operations to highly sophisticated global networks

• Fueled by easier access to product via internet

*Sources: H.R. 32: Stop Counterfeiting in Manufactured Goods Act; Center for Medicines in the Public Interest*
Online pharmacies

- The National Association of Boards of Pharmacy (NABP) has compiled a ‘Not Recommended Sites’ list, which states that >95% of all online pharmacies are violating US public welfare and safety laws.
- Only very few (approximately 30) have NABP Verified Internet Pharmacy Practice Site (VIPPS) accreditation (on-site inspections, prescription mandates, and other standard quality requirements).
- Of the over 8,000 websites reviewed, more than 85% did not require a valid prescription before shipping drugs to customers.

Drug Counterfeiting is Globally Networked
Drugs Smuggled Into the Country
Four Categories of Non-Approved Meds

1. “Generic” Products
2. Alternative Formulations
3. Herbal Formulations
4. Counterfeit Products
1. "Generic" Products

- Non-FDA approved versions of branded pharmaceuticals
- Contain varying amounts of active ingredients
- Often sold at significant price discount to branded products
2. Alternate Formulations

- Reformulated to dissolve more quickly
- Generally sold as lozenge or gel tab
- Make unsupported claims of faster onset
- Volume and source of active ingredient unknown
- Not FDA approved
3. Herbal Formulations

- Purported to be all natural made from plants, herbs or minerals
- No scientific evidence demonstrating efficacy
- May contain ingredients with potentially dangerous side effects
- Marketing claims not rigorously investigated or regulated like FDA pharmaceuticals
- The FDA & FTC have been lax when it comes to policing these so-called sex supplements
- e.g. Enzyte estimated 2004 sales: $240 million

Source: Center for Science in the Public Interest
“Natural” ED Treatments Often Contain Synthetic PDE5-Inhibitors

• The field of herbal medicine has gained popularity & these products regarded as harmless due to their “natural” origin

• 17 commercial formulations of “herbal” or “dietary” supplements marketed for sexual dysfunction were analyzed: 8 of the 17 contained compounds related to synthetic PDE5-inhibitors - sildenafil, tadalafil, vardenafil

• The “adulteration” of natural herbal products with ED drugs or analogues is a growing trend & poses a health threat to patients

Herbal remedies from the internet are dangerous

- Study safety & reliability of internet sites selling “herbal Viagra”
- “Google” search engine: 160,000 hits assessed
  - 88% outlined effectiveness of drugs
  - 70% stated drug ingredients –commonest: yohimbine, ginseng and gingko biloba
  - 21% gave drug side effects e.g. bleeding and cardiac arrhythmia with gingko
  - 21% had medically trained personnel providing information
  - 18% had referenced information

- None of sites met Code of Conduct requirements set by Health on the Net Foundation (body that accredits medical websites)
- Internet sites selling herbal ED remedies unsafe and unreliable

Thurairaja et al, J Urol 2004: 171, 1191A
4. Counterfeit Drug Production

- WHO definition: deliberately and fraudulently mislabeled with respect to identity and source
- The composition of counterfeit drugs is highly variable
  - Sub-potent
  - Supra-potent
  - Mixed with other active ingredients or unknown substances
  - Similar to genuine drug
- Production facilities for counterfeit drugs are frequently unsterile and in uncontrolled environments

Source: WHO
Authentic Products Are Manufactured in Regulated and Inspected Facilities
Counterfeiters’ manufacturing facilities are frequently unsterile
Storage Facilities Inadequate
Counterfeit Viagra Manufactured in Substandard Facilities

Bucket used to mix ingredients in China

Cement mixer used to dye tablets in Egypt
Counterfeit Viagra Factory in Thailand
Tableting Machine in South America
Counterfeitors Labeling Equipment are Now More Sophisticated
An Important Issue for Sexual Health MD’s

- Sexual health products among the most counterfeited
  - In 2004, Pfizer seized 10.1 million counterfeit Viagra tablets
    - 7 times all other Pfizer products combined
  - Additional 1,499kg of bulk sildenafil seized (~28 million tablets)

Sources: WHO
Prime Target of Counterfeiters

• Reasons for buying online PDE5i’s:
  – High cost of prescription medication
  – Embarrassment associated with underlying condition

Most counterfeit PDE5 inhibitors enter the United States drug market via fraudulent websites accessed easily on the internet.

“The internet is just the wild, wild west”
- Bryon A. Liang
Online Sales of Non-Approved “VIAGRA”

- Approximately 2,700 websites selling Viagra-like products
- 12.9 million visitors per month
- Estimated 2.3 million tablets purchased per month

Websites
- “Real” Viagra: 1,734
- Generic: 488
- Alt. Form.: 90
- Herbal: 36

Monthly Sales (000s)
- “Real” Viagra: 390
- Generic: 700
- Alt. Form.: 400
- Herbal: 1200

Source: Cyveillance, Inc.
EAASM “Counterfeiting Superhighway” Research (European Alliance for Access to Safe Medicines)

- Identified and assessed >100 online pharmacies
- 3 phases: finding and inspecting pharmacies, purchasing medicines online, unwrapping and expert analysis

**Is there a named, verifiable pharmacist?**
- Yes: 6.2%
- No: 93.8%

**Is a prescription required for prescription-only medicines?**
- Yes: 9.7%
- No: 90.3%

**Does the pharmacy physically exist?**
- Yes: 15.5%
- No: 84.5%

**Is the website violating intellectual property?**
- Yes: 78.8%
- No: 22.2%

Seized Sildenafil Counterfeits and Imitations in Europe

Source: Data on File. Pfizer, Inc.
Pfizer analyzed 2383 samples seized by authorities worldwide for suspicion of being counterfeit Viagra.

- 626 (26%) were seized in the United Kingdom.
- By spectral analysis, only 85 (14%) samples were authentic.
- 320 (51%) were ordered via the Internet; 264 (83%) of these samples were counterfeit.

Risks to Patients

- **Financial Risks**
  - Lost money
    - Orders often unfulfilled
    - Shipping & consultation fees may offset advertised savings
  - Identity theft
  - Limited legal recourse
- **Safety Risks**
  - No prescription required
    - Inadequate review by online doctors
    - Risk of drug-drug interactions
  - Product quality
    - Incorrect medicine
    - Expired medications
    - Little or no active ingredients
    - Improper storing/distribution
    - Contaminants
    - Lack of package insert

Source: Prevention, February 2004
Aim: Evaluate men who obtain PDE5 inhibitors without healthcare professional (HCP) interaction

Methods: Web-based observational study in UK, Germany, and Italy

Results: Of 11,899 participants; 1,252 (10.5%) reported PDE5 inhibitor use in last six months; 403 (32.3%) without HCP interaction; 65% had ED by IIEF

1/3 of Men Obtaining Treatment for ED are Currently Outside the Healthcare System (HCS)

**Patients Outside the HCS by Country (%)**

<table>
<thead>
<tr>
<th>Country</th>
<th>Outside HCS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>30.6</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>48.4</td>
</tr>
<tr>
<td>France</td>
<td>15.3</td>
</tr>
<tr>
<td>Germany</td>
<td>27.6</td>
</tr>
</tbody>
</table>

**Patients Outside the HCS by Age (%)**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Outside HCS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-40 Years</td>
<td>40.7</td>
</tr>
<tr>
<td>41-60 Years</td>
<td>29.0</td>
</tr>
<tr>
<td>≥61 Years</td>
<td>14.6</td>
</tr>
</tbody>
</table>

Men were considered outside the HCS if they had no contact with a healthcare professional to diagnose, prescribe, or provide treatment for ED. Treatment was outside the HCS if it was acquired without prescription via the Internet, a mail-order pharmacy, or from a friend/acquaintance or partner.

Source: Banks I et al. Presented at: Joint Congress of the European and International Societies for Sexual Medicine (ESSM/ISSM); December 7-11, 2008; Brussels, Belgium. Poster MP-026.
Men who bypassed the healthcare system were FOUR times more likely to purchase an imitation PDE5i

Purchases of Imitation PDE5-Inhibitors by Men Who Interacted Within the HCS vs Those Who Did Not Interact Within the HCS

<table>
<thead>
<tr>
<th>Within HCS</th>
<th>Outside HCS</th>
</tr>
</thead>
<tbody>
<tr>
<td>93%</td>
<td>72%</td>
</tr>
</tbody>
</table>

Source: Banks I et al. Presented at: Joint Congress of the European and International Societies for Sexual Medicine (ESSM/ISSM); December 7-11, 2008; Brussels, Belgium. Poster MP-026.
72% of men who bypassed the healthcare system to obtain treatment had ED

Severity of ED*

- 72%: Mild
- 43%: Moderate
- 25%: Severe
- 4%: Outside HCS

*ED severity was determined with the Massachusetts Male Aging Study question.

PDE5 inhibitor use without HCP interaction is a public health concern:

1. Men expose themselves to risk of unapproved generics and unnecessary risk of counterfeit medications
2. These future patients miss the opportunity to receive information on correct product use and contraindications
3. These men bypass opportunity to receive appropriate health information and medical follow-up for unrecognized CV disease. Hence, delay in diagnosis of cardiac risk factor e.g. HTN, DM, hyperlipidemia, etc

Reasons Men with ED May Not Consult a Healthcare Professional

% Total Respondents Per Country Who DID NOT Consult a Physician

- **Lack of perception of problems**
- **Thinks issue is not a medical problem**
- **Embarrassment**
- **Problem with access to or affordability of medical care**


• 1,144 men who reported PDE5i use within the past year
• 22.0% of men obtained PDE5i via the Internet.
• Counterfeit drugs survey in Japan and Thailand revealed that 55.4% of the PDE5i obtained via the Internet are counterfeits
• Lower awareness of better general health, lower awareness of ED, lower rate of alcohol intake, fear of HCP interview to obtain PDE5i were independent prognostic factors for purchase via the internet

Reasons for Exponential Growth in Drug Fraud and Counterfeiting:

1. Increase in price of prescription medications (PDE5 I’s)
2. Growth of unregulated internet pharmacies
   “The internet is the wild, wild west”
3. Entry of organized crime syndicates

   $1,000 DOWN – returns $20,000 on heroin
   $1,000 DOWN – returns $450,000 on fake Viagra

Legal repercussions not as severe for drug counterfeiting as it is for narcotic charges
Methods to discriminate PDE5 I from counterfeited drugs

- Chromatography
  - Thin layer chromatography (TLC), High pressure liquid chromatography with ultraviolet detection (HPLC-UV), Liquid chromatography with mass spectrometric detection (LC-MS), LC-diode array detection (DAD), Ultra-high-performance liquid chromatography-UV-method (UHPLC)
- X-ray fluoroscopy spectrometry
- Raman spectroscopy
- Near infrared spectroscopy
- Atmospheric solid analysis probe (ASAP)

Deconinck E et al. Talanta. 2012;100:123-133
Sacre PY et al. Journal of Chromatography A. 2011;1218:6439-6447
Between January 1 and May 26, 2008, a total of 150 non-diabetic patients were admitted to 5 hospitals in Singapore with severe hypoglycemia

- All patients except one were male
- Ages ranged from 19 to 97 years (median, 51)
- 7 patients comatose caused by severe & prolonged hypoglycemia
- Four subsequently died

Glyburide was detected in blood or urine samples obtained from 127 of these patients (85%).

Glyburide is one of the most widely prescribed oral sulfonylurea drug used to treat type II diabetes

HPLC analysis of counterfeit drug (A) and Pfizer manufactured drug (B)

HPLC: high-performance liquid chromatography

On specific questioning, 45 patients (30%) admitted ingesting illegal sex-enhancement drugs before the onset of hypoglycemia.

Samples of the counterfeit drugs were obtained from patients and from drugs seized in police raids.

The counterfeit drugs were sold as Viagra, Cialis, and 3 herbal preparations for ED (Power 1 Walnut, Santi Bovine Penis Erecting Capsule, and Zhong Hua Niu Bian).

Four drugs were analyzed by HPLC.

- In addition to containing sildenafil, some of the counterfeit drugs contained tadalafil and sibutramine.

# Internet-Ordered Viagra (Sildenafil Citrate) Is Rarely Genuine

Neil Campbell,* John P. Clark,* Vera J. Stecher, PhD,* and Irwin Goldstein, MD†

*Pfizer Inc, New York, NY, USA; †Alvarado Hospital, San Diego, CA, USA

## Table 1  Analysis of ordering and products received from 22 unique Web sites purporting to sell Viagra

<table>
<thead>
<tr>
<th>Web site</th>
<th>Prescription required?</th>
<th>Price per tablet ($)</th>
<th>Postal origin</th>
<th>PI sheet included?</th>
<th>Blister intact on all tablets?</th>
<th>Test result</th>
<th>API (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><a href="http://www.accessrx.com">http://www.accessrx.com</a></td>
<td>No</td>
<td>29.67</td>
<td>United States</td>
<td>No</td>
<td>Yes</td>
<td>Authentic</td>
<td>N/A</td>
</tr>
<tr>
<td><a href="http://www.onlinepharmacy.com">http://www.onlinepharmacy.com</a></td>
<td>No</td>
<td>5.95</td>
<td>United States</td>
<td>No</td>
<td>Yes</td>
<td>Counterfeit</td>
<td>30</td>
</tr>
<tr>
<td><a href="http://www.atlanticdrugs.com">http://www.atlanticdrugs.com</a></td>
<td>No</td>
<td>33.00</td>
<td>United States</td>
<td>No</td>
<td>*</td>
<td>Authentic</td>
<td>N/A</td>
</tr>
<tr>
<td><a href="http://www.topills.com">http://www.topills.com</a></td>
<td>No</td>
<td>12.50</td>
<td>Canada</td>
<td>No</td>
<td>No</td>
<td>Counterfeit</td>
<td>40</td>
</tr>
<tr>
<td><a href="http://www.videochron.com">http://www.videochron.com</a></td>
<td>No</td>
<td>3.28</td>
<td>India</td>
<td>Yes</td>
<td>No</td>
<td>Illegal generic</td>
<td>N/A</td>
</tr>
<tr>
<td><a href="http://www.erektilodysfunktion-pills.com">http://www.erektilodysfunktion-pills.com</a></td>
<td>No</td>
<td>15.63</td>
<td>China</td>
<td>Yes</td>
<td>No</td>
<td>Counterfeit</td>
<td>35</td>
</tr>
<tr>
<td><a href="http://www.directpharma.net">http://www.directpharma.net</a></td>
<td>No</td>
<td>11.20</td>
<td>Hong Kong</td>
<td>No</td>
<td>No</td>
<td>Counterfeit</td>
<td>35</td>
</tr>
<tr>
<td><a href="http://www.buyingviagra.us">http://www.buyingviagra.us</a></td>
<td>No</td>
<td>9.06</td>
<td>Hong Kong</td>
<td>Yes</td>
<td>No</td>
<td>Counterfeit</td>
<td>45</td>
</tr>
<tr>
<td><a href="http://www.gerrygriffin.com/viagra">http://www.gerrygriffin.com/viagra</a></td>
<td>No</td>
<td>8.66</td>
<td>Hong Kong</td>
<td>Yes</td>
<td>No</td>
<td>Counterfeit</td>
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</tr>
<tr>
<td><a href="http://www.v-medical.com/viagra.html">http://www.v-medical.com/viagra.html</a></td>
<td>No</td>
<td>12.10</td>
<td>United States</td>
<td>No</td>
<td>No</td>
<td>Counterfeit</td>
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</tr>
<tr>
<td><a href="http://www.buyviragryou.com">http://www.buyviragryou.com</a></td>
<td>No</td>
<td>12.90</td>
<td>Hong Kong</td>
<td>No</td>
<td>No</td>
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<td>30</td>
</tr>
<tr>
<td><a href="http://www.doctor-approved.org">http://www.doctor-approved.org</a></td>
<td>No</td>
<td>5.10</td>
<td>Hong Kong</td>
<td>Yes</td>
<td>No</td>
<td>Counterfeit</td>
<td>30</td>
</tr>
<tr>
<td><a href="http://www.viagra.gd">http://www.viagra.gd</a></td>
<td>No</td>
<td>9.06</td>
<td>Hong Kong</td>
<td>Yes</td>
<td>No</td>
<td>Counterfeit</td>
<td>40</td>
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<tr>
<td><a href="http://www.viagra.buy.cc">http://www.viagra.buy.cc</a></td>
<td>No</td>
<td>9.15</td>
<td>United States</td>
<td>No</td>
<td>No</td>
<td>Counterfeit</td>
<td>40</td>
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<tr>
<td><a href="http://www.viagra.ac">http://www.viagra.ac</a></td>
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<td>12.50</td>
<td>Hong Kong</td>
<td>No</td>
<td>No</td>
<td>Counterfeit</td>
<td>35</td>
</tr>
<tr>
<td><a href="http://fr.pharmall.com">http://fr.pharmall.com</a></td>
<td>No</td>
<td>21.75</td>
<td>United Kingdom</td>
<td>Yes</td>
<td>Yes</td>
<td>Authentic</td>
<td>N/A</td>
</tr>
<tr>
<td><a href="http://de.pharm4all.com">http://de.pharm4all.com</a></td>
<td>No</td>
<td>18.50</td>
<td>United Kingdom</td>
<td>Yes</td>
<td>Yes</td>
<td>Authentic</td>
<td>N/A</td>
</tr>
<tr>
<td><a href="http://www.buyviagra1.com">http://www.buyviagra1.com</a></td>
<td>No</td>
<td>7.37</td>
<td>United States</td>
<td>No</td>
<td>Yes</td>
<td>Counterfeit</td>
<td>30</td>
</tr>
<tr>
<td><a href="http://www.adventuregamingstl.org/viagra.aspx">http://www.adventuregamingstl.org/viagra.aspx</a></td>
<td>No</td>
<td>12.50</td>
<td>Hong Kong</td>
<td>No</td>
<td>No</td>
<td>Counterfeit</td>
<td>40</td>
</tr>
<tr>
<td><a href="http://www.buy-viagra-online.me.uk">http://www.buy-viagra-online.me.uk</a></td>
<td>No</td>
<td>10.61</td>
<td>Hong Kong</td>
<td>No</td>
<td>Yes</td>
<td>Counterfeit</td>
<td>35</td>
</tr>
<tr>
<td><a href="http://www.medical-place.com">http://www.medical-place.com</a></td>
<td>No</td>
<td>12.50</td>
<td>Hong Kong</td>
<td>No</td>
<td>Yes</td>
<td>Counterfeit</td>
<td>35</td>
</tr>
<tr>
<td><a href="http://www.buy-viagra.co">http://www.buy-viagra.co</a></td>
<td>No</td>
<td>16.13</td>
<td>Hong Kong</td>
<td>No</td>
<td>Yes</td>
<td>Counterfeit</td>
<td>30</td>
</tr>
</tbody>
</table>

*Not a blister; received as a vial of three loose tablets

API = active pharmaceutical ingredient; N/A = not applicable; PI = product information
77% counterfeit, 18% authentic, and 5% illegal
97 samples claiming to contain sildenafil, tadalafil, or vardenafil seized or purchased from online pharmacies by Italian authorities

All the samples purchased online were easily obtained without a physician’s prescription

Analyzed by visual inspection, liquid chromatography, Infrared Spectroscopy, Differential Scanning Calorimetry, and Thermo-Gravimetry

Composition of illegal substances

- Excipients different from those in the original medicines: 80%
- Presence of non-pharmaceutical excipients: 17%
- Presence of non-declared excipients that should be declared on label: 20%

Original 7%
Illegal 54%
Counterfeit 24%

OOS = Out of specification

Counterfeit Medications: What can WE do about it?

- Patients
- Pharmaceutical Companies
- Regulatory Authorities
- Healthcare Professionals
Efforts to Control Counterfeit Distribution

- PDE5 inhibitor Companies
  - Working with regulatory and law enforcement authorities
  - Distinctive Packaging
  - Holographic Security Foil
  - 2D Barcode
  - Radio Frequency Identification (RFID) tags
- World Health Organization (WHO)
  - In 2006, created a global coalition of stakeholders called IMPACT (International Medical Products Anti-Counterfeiting Taskforce), which aims to build coordinated networks across and between countries in order to halt the production, trading, and selling of fake medicines around the globe

Radiofrequency identification tags

The unfunded cost of implementation of FDA e-pedigree mandates in the USA have been estimated to range from $84,000 for individual pharmacies to $1.3 billion for large-chain pharmacies and may present significant barriers to RFID adoption.

Paxton M. Clin Pharmacol Ther. 2011;89:316-319
FDA has significantly increased the number of counterfeit drug cases it has initiated and prosecuted.

Aimed at intercepting product before entering the physical drug supply chain.

Counterfeit drug cases opened by FDA per year

Source: FDA
Suggested trilateral working group

Educating Consumers on the Risks of Counterfeit Meds

• FDA launched significant public education campaign
  – Magazine PSAs reaching 4.5 million readers
  – 4.6 million education leaflets distributed by retail pharmacies
  – News articles reaching 9.5 million consumers
  – Consumer website: www.fda.gov/counterfeit
  – Pharmacist education program in development

• PDE5 I companies have educated potential ED patients on risks of buying non-FDA approved products
  – Sponsored search engine results educate consumers
  – e.g. Viagra.com features extensive information on risks of fake Viagra
Preventing counterfeiting: What patients can do

- Be familiar with size, shape, color, taste, and odor of medications
- Be suspicious of drugs with an unusually low price
  - “If the price is too good to be true, it probably isn’t!”
- Be suspicious of online pharmacies and/or any vendor that does not provide a physical address & telephone landline
- Look for evidence of a removed or switched product label and/or subtle changes in packaging, including alterations in the expiration date
- Report new side effects to a pharmacist and prescribing health professional, especially unexpected side effects
What You the Physician Can Do

• Continue to advocate treatment of sexual health conditions
  – Support efforts to maintain consumer access to sexual health medicines
  – Encourage non-specialists to probe for sexual concerns

• Educate patients on the risks of counterfeit & other non-FDA approved products

• Remind them to only purchase from a VIPPS-certified pharmacy if they want to fill their prescription online

• Report any suspected cases of counterfeit medicines to FDA
  – http://www.fda.gov/medwatch
Summary: What can be done about Counterfeit PDE5 Inhibitors

- Recognize that this is truly an international problem
- Implement a worldwide consensus on what is counterfeit
- Increase penalties and fines
- Educate physicians on the real dangers of counterfeit drugs and the need to take a stand against them
- Inform patients of the risks of purchasing medications from internet pharmacies
Pharmacological risks posed by counterfeit PDE5-inhibitors are significant

<table>
<thead>
<tr>
<th>Direct Risks</th>
<th>Indirect Risks</th>
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<tbody>
<tr>
<td>Presence of unknown pharmaceutically active ingredients and/or impurities may lead to undesirable and serious side effects or even death</td>
<td>Unsupervised use of PDE5-inhibitors, particularly by men with ED and common comorbid conditions (e.g., hypertension, dyslipidemia, diabetes) may incur</td>
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<tr>
<td>Dosage variability and dosage mislabeling may lead to accidental overdose</td>
<td>Significant risk of morbidity or mortality</td>
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<tr>
<td>Incorrect or incomplete descriptions of product composition create substantial risk for drug-drug interactions</td>
<td>Missed opportunity to address underlying conditions</td>
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<tr>
<td>Minimal or incorrect guidance about contraindications may lead to serious side effects</td>
<td>No basis for determination of drug efficacy or guidance for future use</td>
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<tr>
<td>Addressing side effects caused by an unknown product is difficult and may be dangerous</td>
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BP Oil Spill 2010
Counterfeit drugs are a significant threat to public health. In most studies of the content of counterfeit drugs, the counterfeit product does not contain the amount or type of drug claimed by the product packaging. In many cases, the counterfeit drug contains pharmacological substances not named by the product’s packaging, some of which are illegal and dangerous. Deaths and serious illnesses have been caused by the presence of unnamed pharmacological products in counterfeit drug products. It is impossible for a patient or a healthcare practitioner to know whether or not the stated content of a counterfeit drug is accurate or whether dangerous substances have been added to a product.