The Importance of Quality in Our Medicines Regardless of the Source

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Alliance for Safe Online Pharmacies
ASOP Global Illegal Online Drug Sales Research Symposium
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www.fda.gov
Outline

• Pharmaceutical Quality
• U.S. FDA’s Office of Pharmaceutical Quality (OPQ)
• OPQ Research
  – Surveillance of Internet Drug Products
  – Rapid Screening Research
• Conclusions
Pharmaceutical Quality
Pharmaceutical Quality

A quality product of any kind consistently meets the expectations of the user.

Drugs are no different... regardless of the source.
Patients expect safe and effective medicine with every dose they take.
Pharmaceutical quality is consistently meeting standards that ensure every dose is safe and effective, free of contamination and defects.
A History of Quality Events

Congress and FDA have acted because companies failed to adequately ensure quality

<table>
<thead>
<tr>
<th>Year</th>
<th>Event Description</th>
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<tr>
<td>1938</td>
<td>&gt;100 deaths from elixir sulfanilamide</td>
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<td></td>
<td>1938 Food, Drug, and Cosmetic (FD&amp;C) Act</td>
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<td></td>
<td>Safety studies required for new drugs</td>
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<td>1962</td>
<td>Children born with severe birth defects from thalidomide</td>
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<td>1962 Kefauver-Harris Amendments to the FD&amp;C Act</td>
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<td>Need to prove that drugs are safe and effective</td>
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<td>2015</td>
<td>Serious injuries and deaths from global heparin crisis</td>
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<td>FDA establishes Office of Pharmaceutical Quality</td>
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<td>Integrates functions and elevates FDA’s commitment to quality</td>
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I watched my husband and my best friend slip away before my eyes.

As a nurse, I thought that I would be there to save my husband from any errors, but I guess I was naïve.

I never thought the life-saving medication we were relying on might be contaminated.
U.S. FDA’s Office of Pharmaceutical Quality
Pharmaceutical quality is our *shared* goal of assuring consistently safe and effective drugs are available to patients and consumers.

Pharmaceutical quality is what gives them confidence in their *next* dose.

**Mission**
OPQ assures that quality medicines are available to the American public

**Vision**
OPQ will be a global benchmark for regulation of pharmaceutical quality

**Motto**
*One Quality Voice*
Office of Pharmaceutical Quality

Across the globe… Across the lifecycle… Across product classes…

Policy Assessment Inspection Surveillance Research

OPQ

Development Premarket Postmarket

new drugs compounded drugs over-the-counter drugs biosimilars

biologics

generics
OPQ

Immediate Office
Michael Kopcha
Office Director
Lawrence Yu
Deputy Director

Office of Testing and Research (OTR)
Sau (Larry) Lee

Office of Surveillance (OS)
Cindy Buhse

Office of Process and Facilities (OPF)
Lawrence Yu (acting)

Office of Program and Regulatory Operations (OPRO)
Don Henry (acting)

Office of Program and Regulatory Operations (OPRO)
Ashley Boam

Office of Program and Regulatory Operations (OPRO)
Don Henry (acting)

Office of New Drug Products (ONDP)
Giuseppe Randazzo (acting)

Office of Program and Regulatory Operations (OPRO)
Ashley Boam

Office of Lifecycle Drug Products (OLDP)
Susan Rosencrance

Office of Program for Pharmaceutical Quality (OPPQ)
Ashley Boam

Office of Biotech Products (OBP)
Steven Kozlowski

Manages the business processes associated with quality assessments and facility inspections

Develops policies, standards, and guidance documents related to drug product quality

Performs quality assessment of drug substance & product (INDs, NDAs, ANDAs, BLAs, supplements)

Performs quality assessment of manufacturing process & facilities

Monitors information about the entire inventory of CDER-regulated sites and products

Performs research to support scientific standards/policies & surveillance/investigational testing

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One Quality Voice

CDER
Office of Pharmaceutical Quality

CDER
Office of Compliance

Office of Regulatory Affairs
Pharma Program

One Quality Voice
Alex Azar • @SecAzar • Mar 7
I spent some time at @US_FDA and @FDA_Drug_Info yesterday. I’m continually inspired by the great work being done by the talented men & women of #HHS.
Centers of Excellence (COEs)

- Immunology
- Manufacturing Science & Innovation
- Pharmaceutical Analysis & Characterization
- Infectious Disease & Inflammation
- Tumor Biology
Surveillance of Internet Drug Products
Quality of Internet Drug Products

• Project assessing the quality (identity, strength and purity) of “high risk” prescription drug products offered for sale over the internet
  – E.g., narrow therapeutic index, black box warnings, etc.
  – Undercover buys of unapproved prescription drug products from illegal online pharmacies
  – Also prescription drug products collected at courier hub facilities that do not appear to meet the prescription drug regulatory requirements

• Analyzed these products using USP compendial methods for ID, assay, and impurities
Surveillance of Internet Drug Products

• Over a three year period, **approximately ~10%** of the samples failed to meet specification criteria

• FDA is taking appropriate regulatory actions on products that have been found to be adulterated, misbranded and/or unapproved
Rapid Screening Research
Conventional Sampling Process

- Thousands of packages enter the US through International Mail Facilities (IMFs) every day
- FDA is able to physically inspect less than 0.06% of packages presumed to contain drug products shipped through the IMFs
- It can take days or weeks to get sampling results
  - Must be sent to labs for testing
  - During that time products have to be held at IMFs
- Limited space/resources restrict the number of products that can be tested by the agency
Rapid Screening Technologies

- OPQ has an initiative to develop screening methods directly on-site at import locations
- Uses portable instrumentation with the goal of providing faster results with similar reliability and accuracy as lab methods
- Developed a method for a field deployable screening device called an ion mobility spectrometer (IMS)
  - Common applications: detection of explosives, illicit drugs, chemical warfare agents
  - Compares the chemical signature of an unknown substance against the chemical signatures of known compounds
On-Site Screening Process

- After a few minutes of prep, screening a sample usually takes <30 seconds
- Inspectors do not need to be able to analyze the data to use the device
IMS Pilot Study

• A six-month pilot study with the Office of Enforcement and Import Operations and the Office of Regulatory Affairs deployed the device at two international mail facilities

• Used custom-built libraries with chemical signatures of weight loss or sexual enhancement drugs

• Screened imported supplement samples for undeclared pharmaceutical ingredients

• The pilot was a success: the method was reliable and valid

FURTHER:

• 65% tested positive for undeclared ingredients
  • ~90% for sexual enhancement supplements

*Results were confirmed in FDA lab
IMS @ IMFs

• Samples no longer need to be sent to an FDA lab
  – Results directly in the field can be used to refuse entry of a product (based on the appearance of a violation of the FD&C Act)
  – This is a significant milestone for our Rapid Screening Research Program

• We are now expanding the use of IMS instruments to additional IMFs
  – Our goal is to employ these devices at every IMF

• We are developing new pharmaceutical libraries to screen active ingredients in approved or counterfeit drug products
  – Opioids
FDA Response to Fraudulent Products

• Refuse Admittance (imports)
• Internet and Social Media Warnings
• Public Notifications, Enforcement, and Recall Information
• Criminal Convictions
Conclusions
Organizations OPQ Regularly Engages

- U.S. Pharmacopeial Convention (USP)
- ASTM International (ASTM)
- The Pharmaceutical Research and Manufacturers of America (PhRMA)
- Association for Accessible Medicines [formerly Generic Pharmaceutical Association (GPhA)]
- Biotechnology Industry Organization (BIO)
- International Pharmaceutical Excipients Council (IPEC)
- American Association of Pharmaceutical Scientists (AAPS)
- Consumer Healthcare Products Association (CHPA)
- International Society for Pharmaceutical Engineering (ISPE)
- Parenteral Drug Association (PDA)
- Product Quality Research Institute (PQRI)
- US National Institute of Standards and Technology (NIST)
- Bulk Pharmaceutical Task Force (BPTF)
- Drug Information Association (DIA)
- Pharma and Biopharma Outsourcing Association (PBOA)
- International Forum on Process Analytical Chemistry (IFPAC)
- Personal Care Products Council (PCPC)

NOT LISTED:

Healthcare professionals/providers
Patients
Consumers
Students...etc.

- American Association of Pharmaceutical Scientists (AAPS)
- International Forum on Process Analytical Chemistry (IFPAC)
- Consumer Healthcare Products Association (CHPA)
- Personal Care Products Council (PCPC)
Drug Quality 101
Curious about the quality of your medications?

Q: What does drug quality mean?
A: A drug product of any kind consistently meets the expectations of the user. Drugs are no different. They must be manufactured using standards that ensure every dose is safe, effective, and able to provide its intended benefit. The FDA assesses all drugs before approval to assure they meet established quality standards.

Q: How does drug quality impact me?
A: Quality is what ensures every dose of your drug is of the appropriate strength—not too weak and not too strong—and free of contamination and defects. It gives you confidence in the next dose you take. Also, problems with drug quality can create shortages, which may make your drug unavailable when you need it.

Q: Does the FDA have the same expectations for the quality of a drug made in the U.S. vs. abroad? Brand-name vs. generic?
A: Yes. The FDA has the same expectations for drug quality whether a drug is made in the U.S. or abroad and whether a drug is brand name or generic. You can see the information online about drug approval and whether the drug is approved by the FDA or another regulatory body.

Q: What should I do if I suspect a problem with the quality of a drug?
A: Even when manufacturers are very vigilant, sometimes quality issues occur after drug approval. You can report suspected quality issues with a drug directly to the FDA using the MedWatch system. Visit www.fda.gov/medwatch to easily fill out the case-reporting form for consumers and patients. You can also discuss any concerns you have with your doctor or pharmacist.

By the Numbers

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<tr>
<th>Nearly 1 in 3</th>
<th>90%</th>
<th>More than 1,300</th>
<th>More than 1,000</th>
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<tr>
<td>Number of drug shortages caused for quality issues related to manufacturing</td>
<td>Percentage of annual reported drug shortages have dropped since 2011</td>
<td>Number of patients still feel the FDA Office of Pharmaceutical Quality is one of the best agencies in the U.S.</td>
<td>Number of generic drugs approved by the FDA in 2016, 2017, and 2018 high</td>
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We can’t do this alone

Pharmacists are on the front line between patients and the drugs they take

Healthcare professionals should talk to patients/consumers who believe they have received or taken counterfeit medicine

Healthcare professionals should report suspect counterfeit drugs in FDA’s MedWatch system
A Shared Responsibility

With a focus on patients and consumers, *together* we can provide them confidence in their *next* dose.
My husband was a fighter until the bitter end. He would’ve given anything for one more day. I know that he would want me to make sure that this doesn’t ever happen to anyone else.

Please do not let his death be in vain.

We, as a family, need to know that some good can come of this tragedy.