U.S. FOOD & DRUG ADMINISTRATION

The Importance of Quality in Our Medicines

Join Us in a Commitment to Quality

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Outline

- **Pharmaceutical Quality: What It Means**
- **U.S. FDA's Office of Pharmaceutical Quality (OPQ)**
- **ENGAGE: Strengthen Partnerships and Engage Stakeholders**
  - Join us in a commitment to pharmaceutical quality!
- **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.


It is what gives patients confidence
in their *next* dose of medicine.

A History of Quality Events

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

1938

>100 deaths from elixir sulfanilamide

1938 Food, Drug, and Cosmetic (FD&C) Act

Safety studies required for new drugs

1962

Children born with severe birth defects from thalidomide

1962 Kefauver-Harris Amendments to the FD&C Act

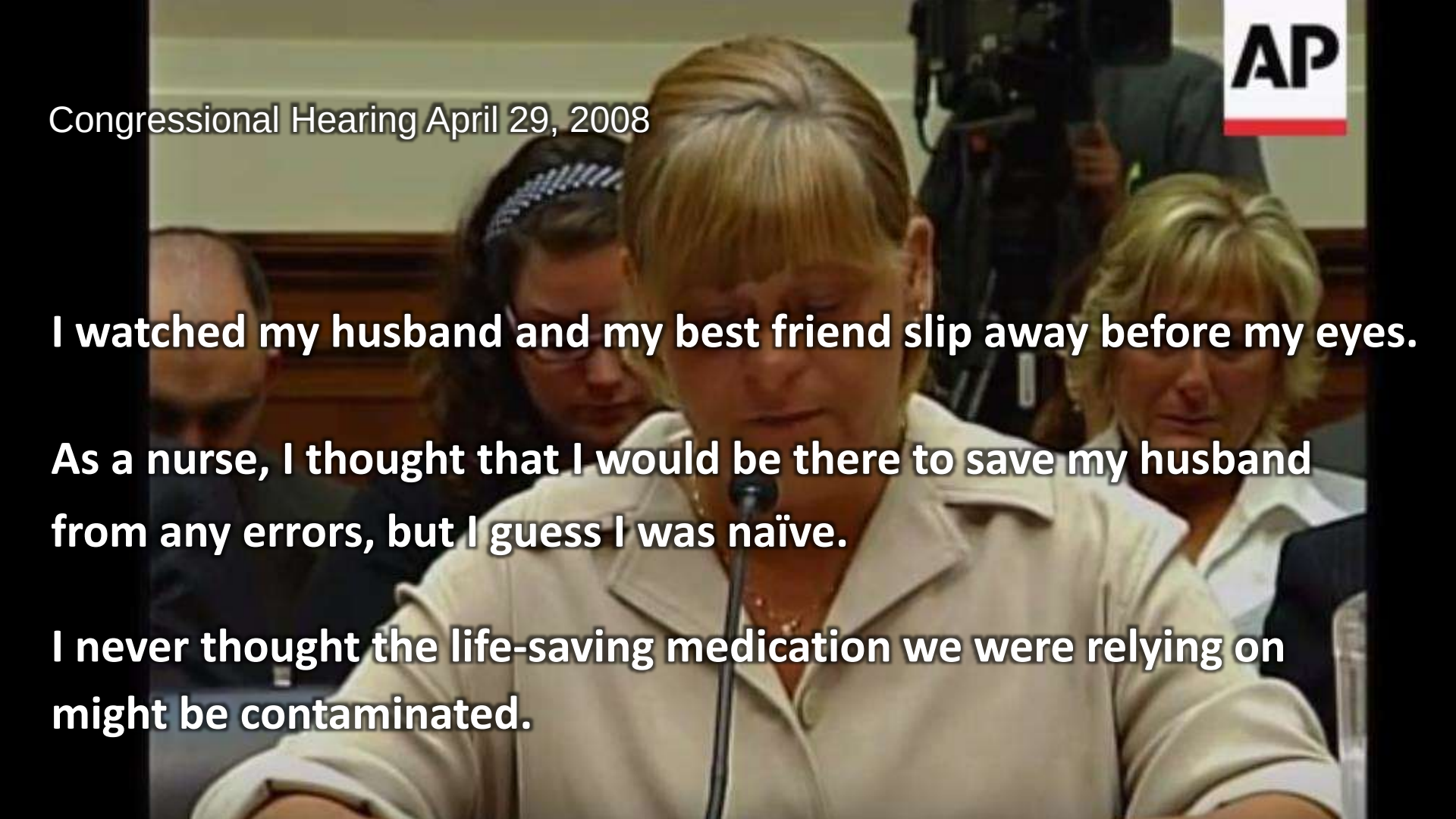
Need to prove that drugs are safe and effective

2015

Serious injuries and deaths from global heparin crisis

FDA establishes Office of Pharmaceutical Quality

Integrates functions and elevates FDA's commitment to quality


Congressional Hearing April 29, 2008
AP
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

Office of Pharmaceutical Quality

One Quality Voice

Print Copies Available

ENGAGE

Strengthen Partnerships and Engage Stakeholders

WE WANT YOU

TO JOIN US IN A COMMITMENT TO QUALITY

Do You Have…

Quality Metrics Programs

Quality Metrics

Many products are made using *Quality Metrics* to monitor quality control and continually improve quality.

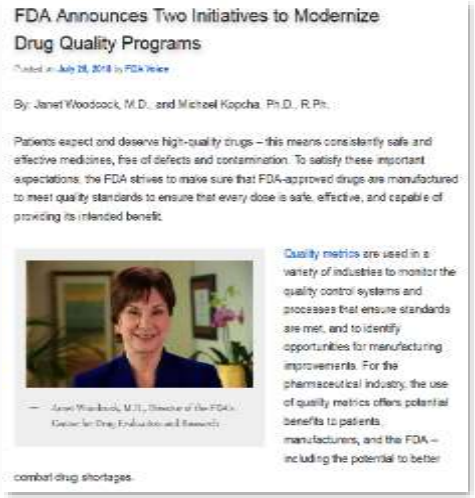
Drugs *should be* no different.

FDA's Quality Metrics Programs

- **Feedback Program**
  - Solicits information from drug manufacturers that are currently using quality metrics programs
  - Any data shared is for demonstration/ informational purposes only
- **Site Visit Program**
  - Provides on-site learning opportunities for FDA staff involved in the FDA Quality Metrics Program
  - Provides stakeholders with the opportunity to explain their advantages and challenges

FDA's Quality Metrics Programs

- **Site Visit Program well-received**
  - Two site visits already completed
  - Visits to six facilities planned
- **Increasing acknowledgement of the value of quality metrics programs**
  - ISPE Culture Excellence Report, PDA Quality Culture Maturity Model and Tool
  - "*PhRMA also supports the current voluntary and pilot program approach to the Quality Metrics program, as well as the on-going research… to investigate… what could be reported to FDA and be beneficial to risk management oversight*."
    - Public Comments to Docket No. FDA-2018-N-3272



FDA Announces Two Initiatives to Modernize Drug Quality Programs

By: Janet Woodcock, M.D., and Michael Kopcha, Ph.D., R.Ph.

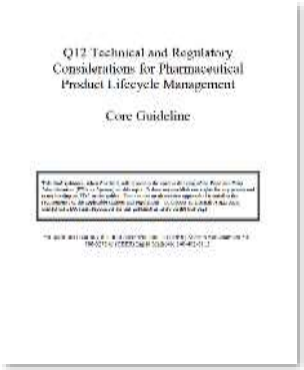
Patients expect and deserve high-quality drugs – this means consistently safe and effective medicines, free of defects and contamination. To satisfy these important expectations, the FDA strives to make sure that FDA-approved drugs are manufactured to meet quality standards to ensure that every dose is safe, effective, and capable of providing its intended benefit.

Quality metrics are used in a variety of industries to monitor the quality control systems and processes that ensure standards are met, and to identify opportunities for manufacturing improvements. For the pharmaceutical industry, the use of quality metrics offers potential benefits to patients, manufacturers, and the FDA – including the potential to better combat drug shortages.

Established Conditions

Established Conditions (ECs)

- **ECs are legally binding information considered necessary to assure product quality**
  - Any change to ECs necessitates a submission to the regulatory authority
- **Although every application contains ECs, FDA *has not specifically indicated* the applicable ECs at the time of approval**
- **Draft ICH Q12 guidance describes how an applicant can specifically identify and propose ECs**



Established Conditions (ECs)

- **2/15/19 - FDA announced a pilot program (FRN) to gain practical experience in ECs**
- **FDA will accept nine requests submitted before 5/30/19 from applicants intending to propose ECs**
- **If interested, submit a written request to the *CDER-OPQ-Inquiries@fda.hhs.gov* mailbox**
  - See FRN (84 FR 4478) for content of request

Emerging Technology Program

Emerging Technology Program

- Supports industry's development and implementation of innovative approaches in **pharmaceutical design and manufacturing**
- Identifies and **resolves potential scientific and policy issues** related to new approaches
  - Enabled the first switch from batch to continuous manufacturing (CM) for an approved drug
- A website and Guidance for Industry are posted

Emerging Technologies

- **CM processes for drug product**
  - Direct compression, dry and wet granulation: CM models for solid orals;

A generic manufacturer using Continuous Manufacturing is engaged with our Emerging Technology program

- **Pharmacy on Demand**
  - Miniaturized, flexible manufacturing platforms using CM technologies

Pre-ANDA Program

Complex Products

COMPLEX…	Example	Products
Active ingredients	Peptides, complex mixtures, natural source products	Glatiramer acetate
Formulations	Liposomes, emulsions	Liposomal formulations
Routes of Delivery	Locally acting drugs such as dermatological products and complex ophthalmological products	Acyclovir cream
Dosage Forms	Transdermal systems, extended release injectables	PLGA microspheres
Drug-Device Combinations	Dry powder inhalers, nasal sprays, transdermal systems	Mometasone nasal spray
Other products	Complexity or uncertainty concerning the approval pathway that would benefit from early scientific engagement	Abuse deterrent opioid formulations

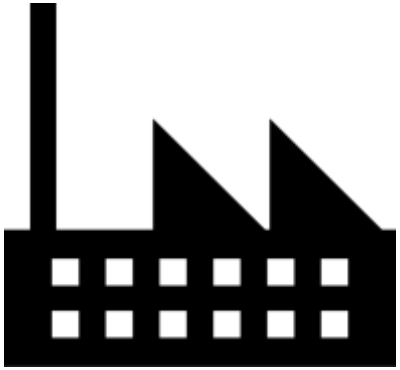
ANDA Program for Complex Products

- **Clarifies regulatory expectations for prospective applicants early in product development**
  - Product Development Meetings
- **Assists applicants in developing more complete submissions**
  - Pre-Submission Meetings
- **Promotes a more efficient and effective assessment process reducing the number of cycles to approval**
  - Mid-Review Cycle Meetings

Site Engagement Program

Site Engagement Program

- **An open discussion and collaboration on manufacturing issues that could impact patients**
  - Helps mitigate or prevent future production problems
- **This is a voluntary program**
- **Initial focus is sites where quality issues could potentially disrupt availability**
  - Not for sites “on the cusp of failure”



Benefits of Site Engagement Program

- **An opportunity for open discussion and collaboration on manufacturing issues**
  - May lead to effective corrective or preventive actions
  - May result in reduced frequency and/or duration of on-site surveillance inspections

Recognition of Voluntary Consensus Standards

Recognition of Voluntary Consensus Standards

- **2/13/19 – Proposed program provides stakeholders the opportunity to propose pharmaceutical quality standards for recognition by the FDA**
  - Voluntary consensus standards related to pharmaceutical quality for informal recognition
  - Would recognize nationally and internationally accepted manufacturing standards for drug quality
- **Draft guidance seeks input on this program**
  Comments due by 4/15/19

CDER's Program for the Recognition of Voluntary Consensus Standards Related to Pharmaceutical Quality

Guidance for Industry

DRAFT GUIDANCE

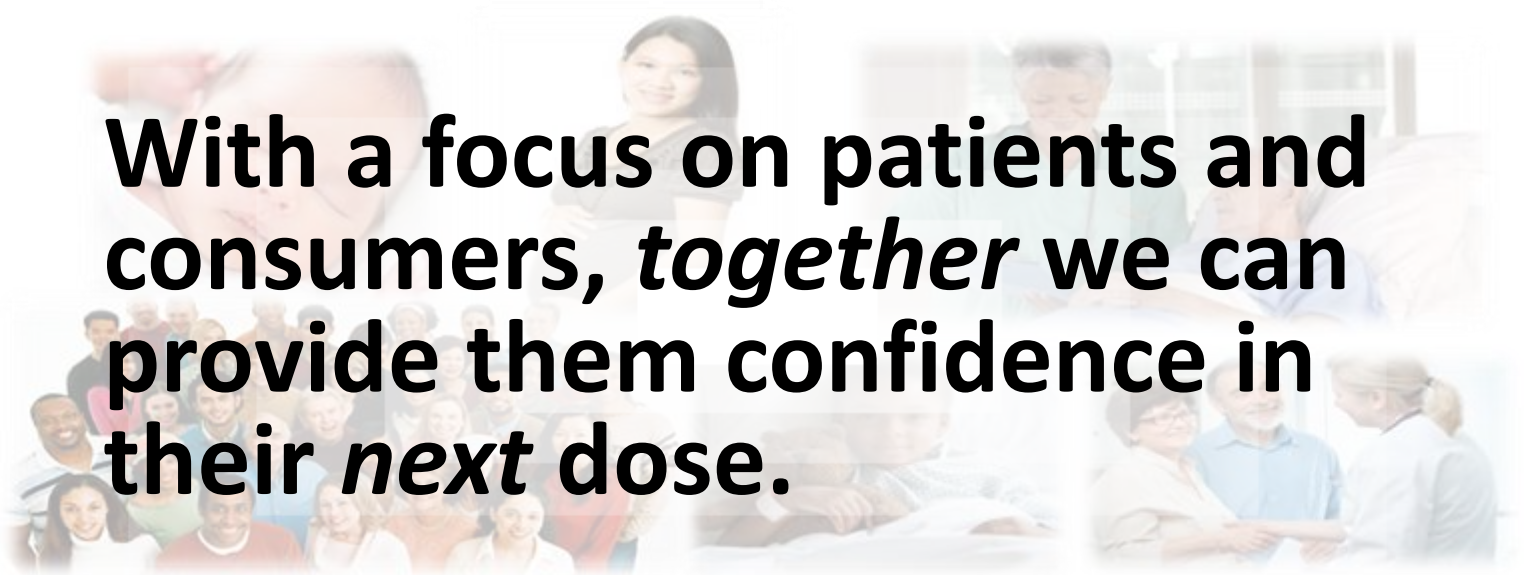
Benefits of Consensus Standards Program

- **Transparency to industry on CDER's thinking on a particular standard**
  - Will help industry compile information for applications
  - Will streamline FDA's assessment
  - Will encourage the development of standards for emerging technologies
- **CDER's first time recognizing informal voluntary consensus standards related to pharmaceutical quality**

Conclusions


We can’t do this alone
Join us in a commitment to pharmaceutical quality

A Shared Responsibility



With a focus on patients and consumers, *together* we can provide them confidence in their *next* dose.


Today
C-SPAN 2


FDA
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