FDA Update

CDR Jeffrey Meng

Program Division Director

Office of Regulatory Affairs (ORA)

Office of Pharmaceutical Quality Operations (OPQO)

Division III

Office of Pharmaceutical Quality Operations

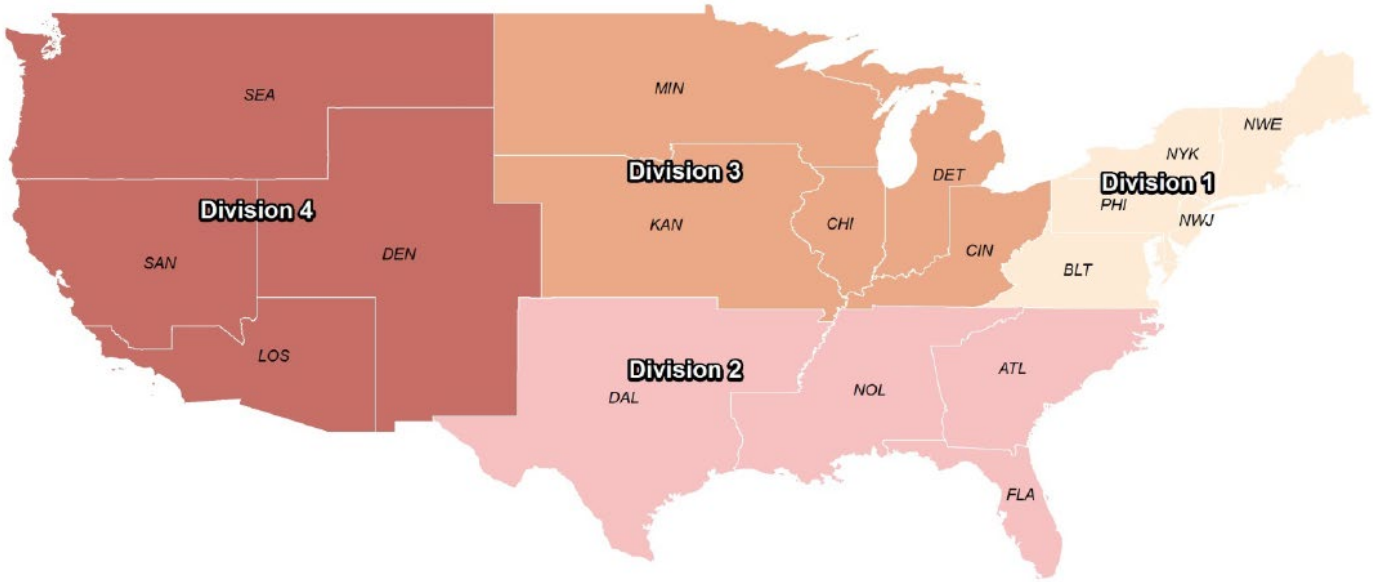
Office of Pharmaceutical Quality Operations

Who We Are

A specialized office to help protect and promote the safety and quality of human and animal drug products.

What We Do

OPQO coordinates domestic and foreign inspectional, investigational and compliance activities.



Division 1 (BLT, NEW, NWJ, NYK, PHI)
Division 2 (ATL, DAL, FLA, NOL, SJN)
Division 3 (CIN, CHI, DET, KAN, MIN)
Division 4 (DEN, LOS, SAN, SEA)
DFPQI - Foreign Pharmaceutical Inspections
DPQP - Pharmaceutical Quality Programs

~430+ employees, including ~200 investigators

OPQO Sites & Products

~7,000 human drug manufacturing sites of obligation (as defined by regulations and policy)

~5,000 Non-MG manufacturers (incl. ~600 hand sanitizer)

~2,000 Medical gas manufacturers (nearly all in U.S.)

43% domestic **57%** foreign

Products

170,000 unique finished doses

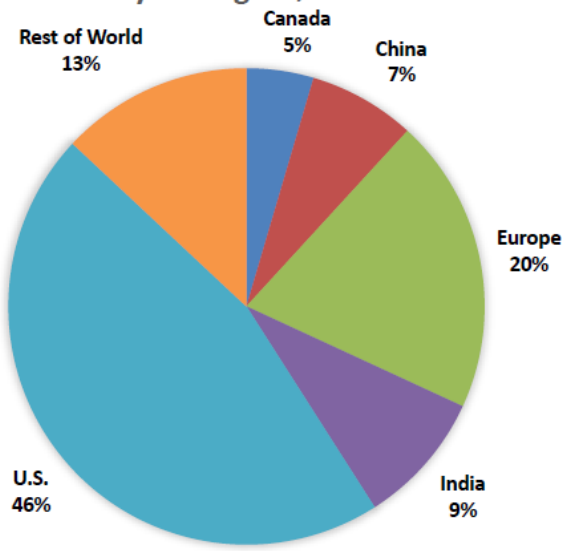
19,000 unique Active Pharmaceutical Ingredients

1,500 unique medical gas

Note: Based on June 2022 CDER Site & Product Catalogs and unique NDCs

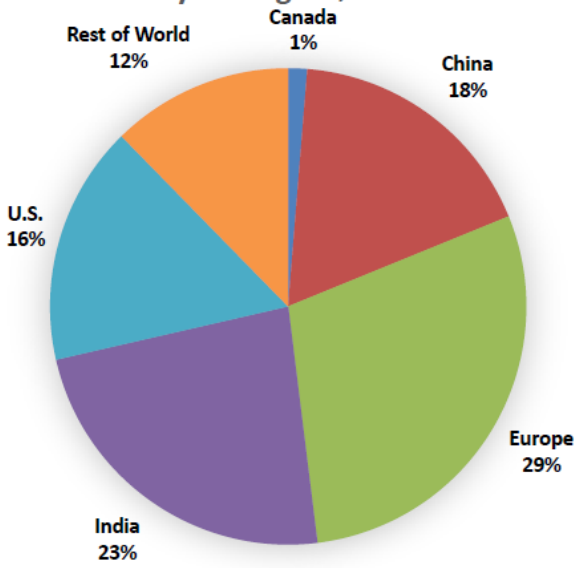
Industry Demographics

Percentage of FDF Manufacturing Facilities for Human Drugs in the U.S. Market by Country or Region, June 2022



>50% of final dosage form manufacturing sites are outside of the U.S.

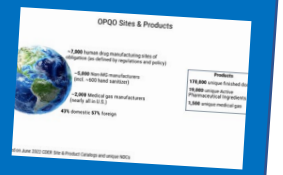
Percentage of API Manufacturing Facilities for Human Drugs in the U.S. Market by Country or Region, June 2022

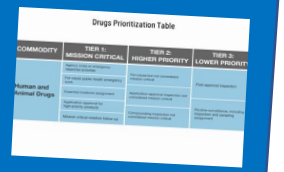


42% of API manufacturing sites are in India & China

agenda

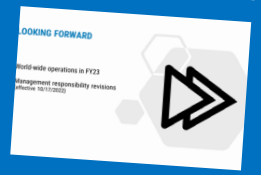

Office of Pharmaceutical Quality Operations
Who We Are
What We Do


OPQO Sites & Products

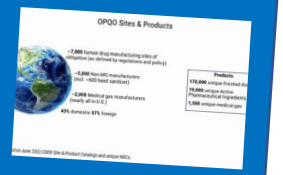

Drugs Prioritization Table
COMMODITY
TIER 1: MISSION CRITICAL
TIER 2: HIGHER PRIORITY
TIER 3: LOWER PRIORITY
Human and Animal Drugs

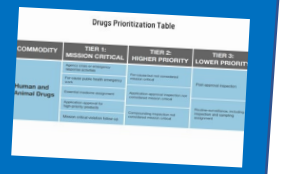

Alternative Tools


FY2022* Regulatory Actions


LOOKING FORWARD

agenda





1. Pandemic Responses, Limitations & Transitions
2. Compliance Trends
3. Looking Forward

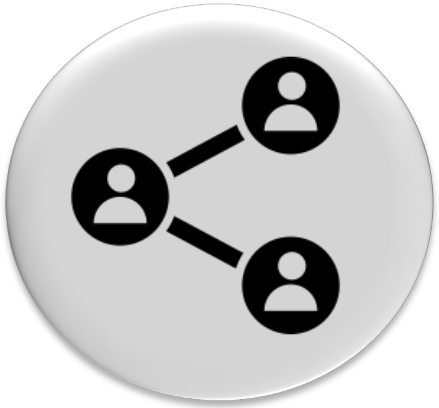
FDA outlines inspection and assessment activities during pandemic, roadmap for future state of operations

Inspectional Priorities

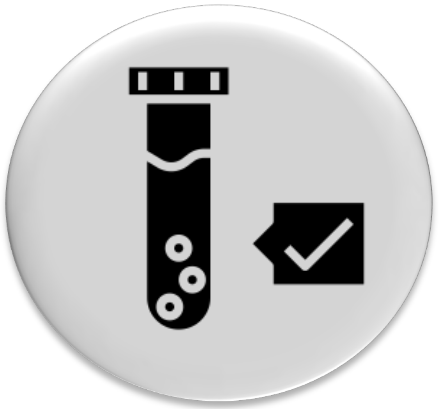
COMMODITY	TIER 1: MISSION CRITICAL	TIER 2: HIGHER PRIORITY	TIER 3: LOWER PRIORITY
Human and Animal Drugs	Agency crisis or emergency response activities	For-cause but not considered mission critical	Post-approval inspection
	For-cause public health emergency work	Application-approval inspection not considered mission critical	
	Essential medicine assignment		Routine-surveillance, including inspection and sampling assignment
	Application-approval for high-priority products	Compounding inspection not considered mission critical	
	Mission-critical violation follow-up		

Alternative Tools

Remote Regulatory Assessments



Mutual Recognition Agreements (MRAs) & Bilateral Information Sharing

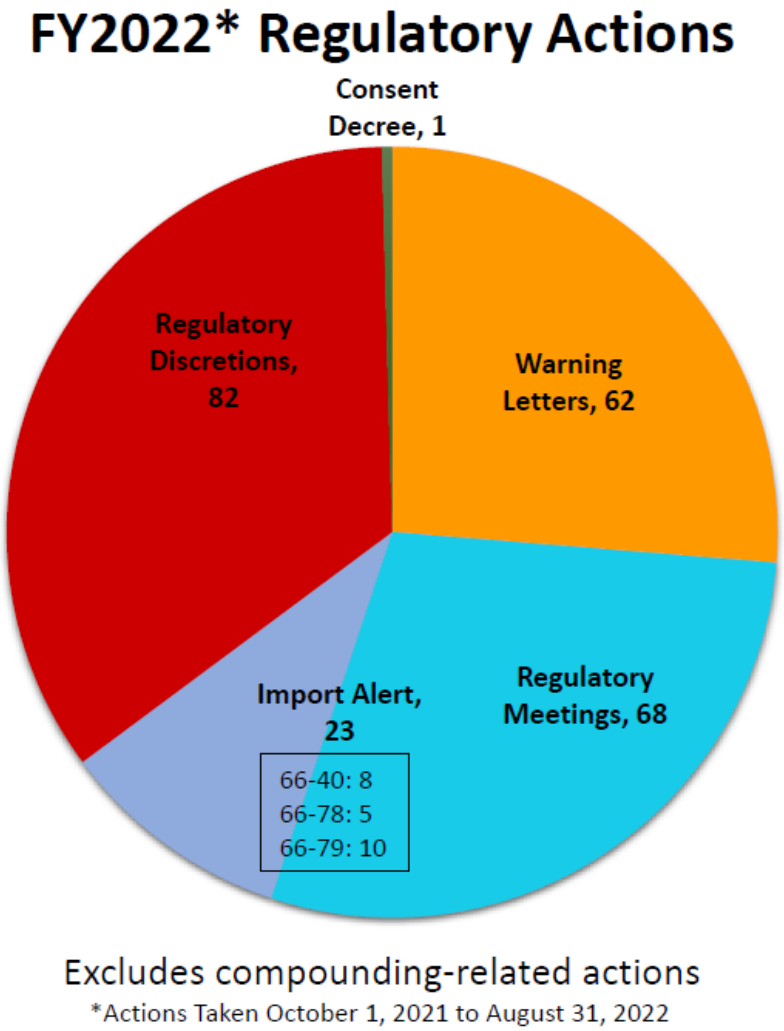


Sampling & Testing

Compliance History & Actions

Enforcement Advisory Tools

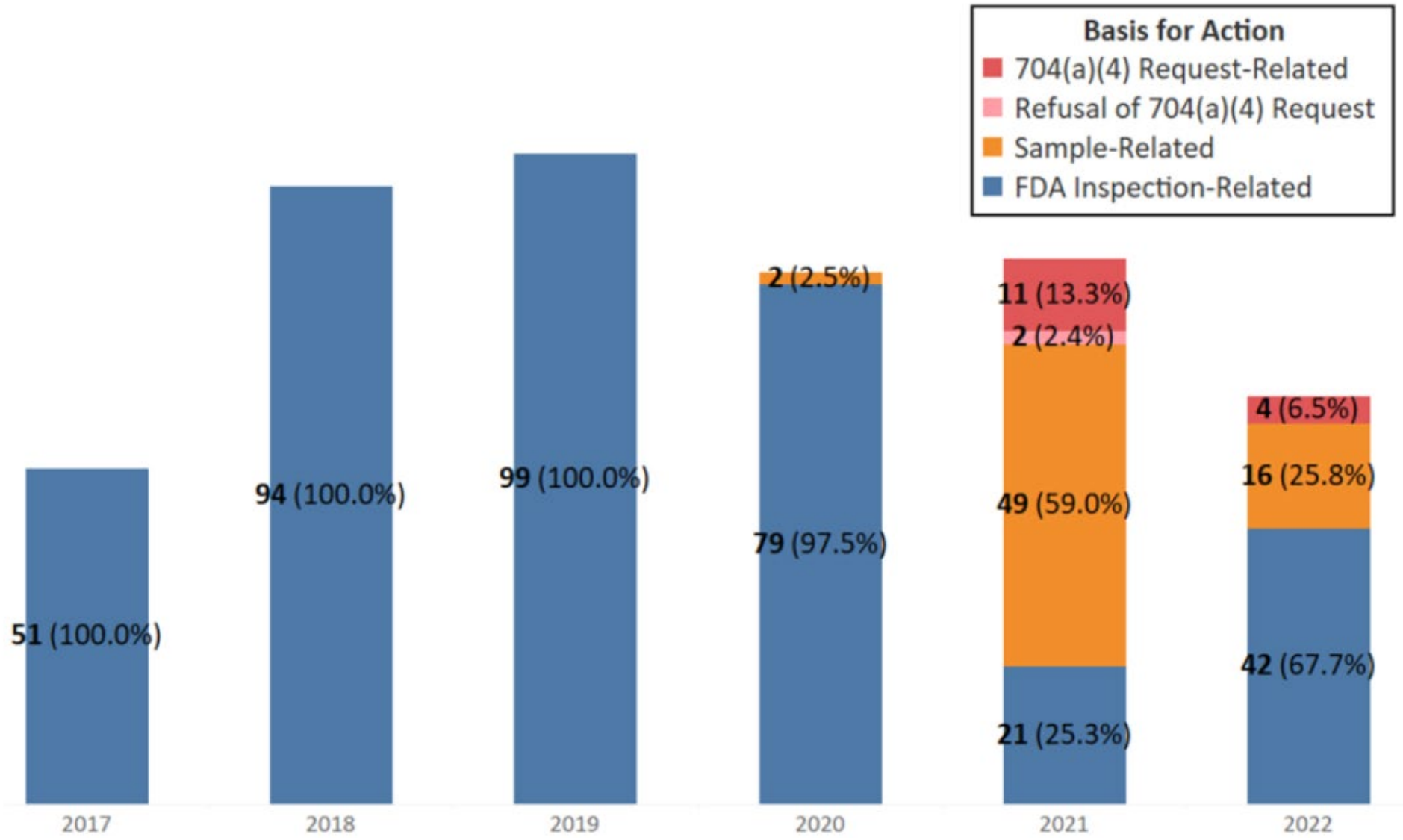
- Regulatory Meetings
- Injunctions
- Consent Decrees
- Import Alerts
- Seizures
- Warning Letters
- Untitled Letters
- Administrative Detention

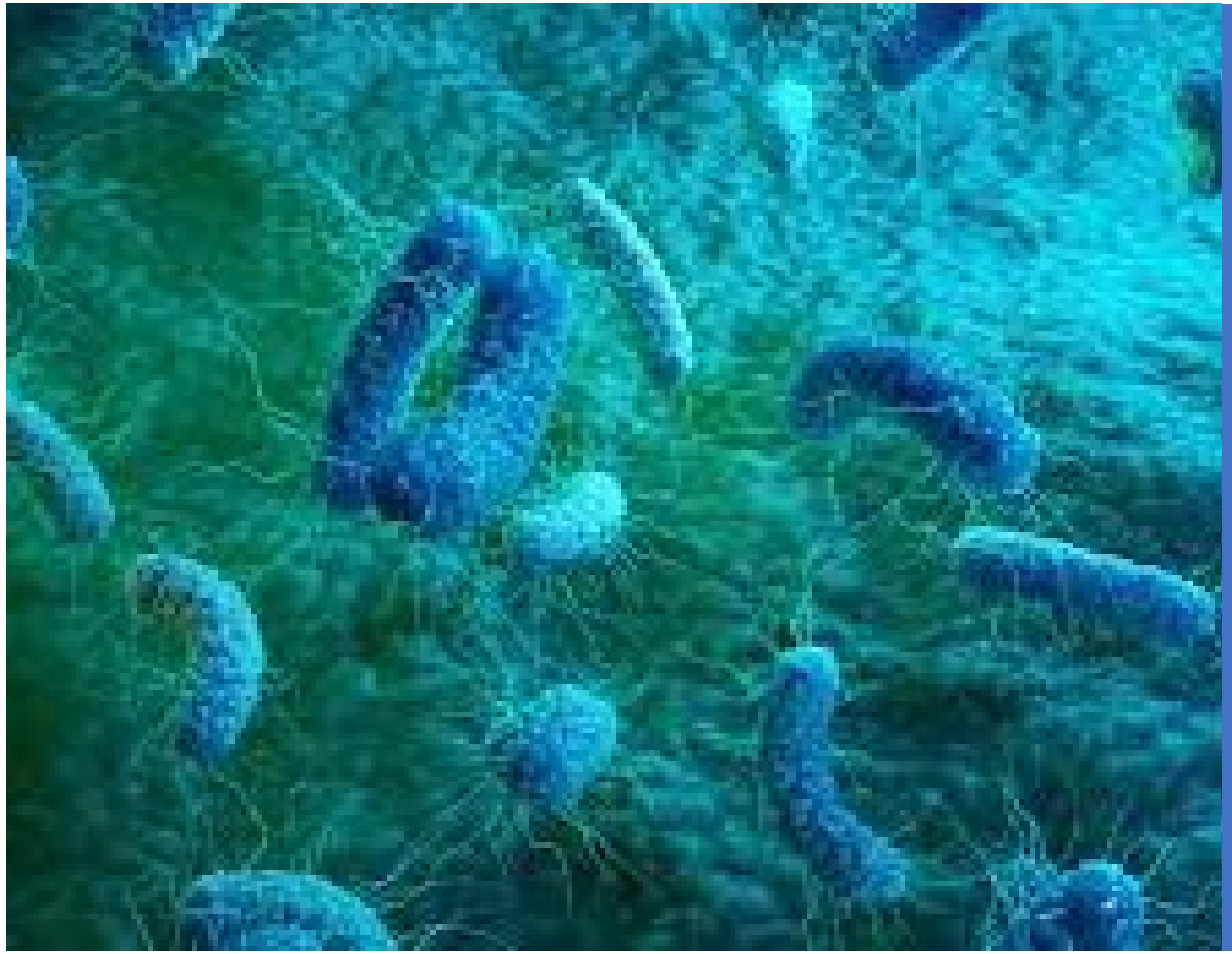


Excludes compounding-related actions

*Actions Taken October 1, 2021 to August 31, 2022

Adulteration Actions Shifts





Burkholderia cepacia complex (BCC)

A group or “complex” of bacteria that can be found in soil and water.

B. cepacia bacteria are often resistant to common antibiotics.

B. cepacia Outbreaks

PharmaTech LLC

Product: Diocto Liquid Stool Softener

Background: CDC and FDA investigate a multi-state BCC outbreak in ventilator patients in 2016 and again in pediatric hospitals in 2017

Problem: BCC contamination in the water system.

Result: Mass recalls of all liquid products in 2016; facility shut down in 2017; criminal prosecution of CEO resulting in 37-month prison sentence in 2022

Contract Manufacturer

Product: Paroex Chlorhexidine Gluconate Oral Rinse

Background: CDC and FDA investigate multi-state BCC outbreak in healthcare settings of seriously ill or immunocompromised patients

Problem: Inadequate investigations, CAPA, equipment design, cleaning and validation, specifications, test methods, etc.

Result: Multiple liquid product recalls in 2020/2021;temporary suspension of drug manufacturing; FDA Warning Letter issued in 2021

FDA advises drug manufacturers that Burkholderia cepacia complex poses a contamination risk in non-sterile, water-based drug products | FDA

Microbiological Quality Considerations in Non-Sterile Drug Manufacturing | FDA

LOOKING FORWARD

- Resume routine world-wide operations in FY23
- Increased focus on management responsibility and risk management

Risk Based Oversight to Ensure Quality and Patient Safety

In 2012, FDASIA amended the definition of CGMP as follows: "[T]he term 'current good manufacturing practice' includes the implementation of oversight and controls over the manufacture of drugs to ensure quality, including managing the risk of and establishing the safety of raw materials, materials used in the manufacturing of drugs, and finished drug products."

Section 711 of FDASIA: Enhancing the safety and quality of the drug supply

What's new?

Updated CPGM 7356.002 eff. 10/17/22

Drug Manufacturing Inspections

- Management oversight of quality system
- Quality risk management program
- Quality oversight of contracted operations and suppliers
- Risk management program for components
- Lifecycle control strategies for hazardous impurities
- Ongoing statistical evaluations to identify unacceptable process variability

Updated CPGM 7346.832 eff. 10/17/22

Preapproval Inspections

- ICH Q12
  - Established Conditions (EC's)
  - Post-approval Change Management Protocol
  - Product Lifecycle Management Document
- Assessing EC's within Change Management / PQS
- Product lifecycle risk management
- Objective 4: Commitment to Quality in Pharmaceutical Development
  - Pharmaceutical Development Program
  - Senior Management Commitment to Quality
  - Multidisciplinary Integrated Development Team
  - Quality Risk Management in Development

Trending Today

- **NDC Proposed Rule**
  FDA is running out of 10-digit NDCs. In July 2022, FDA proposed a rule that would adopt a single, uniform 12-digit format for NDCs.
  See Docket No. FDA-2021-N-1351 for details.

- **Quality Metrics (QM)**
  Revised draft Guidance for Industry entitled "Submission of Quality Metrics Data"
  See Docket No. FDA-2022-N-0075 for details

- **Quality Management Maturity (QMM)**
  See CDER QMM website for details
  See Public Advisory Committee meeting Nov 2, 2022

- **KASA**
  See FDA Industry site and Standardizing Quality Submissions June 2022 Presentation
  See Public Advisory Committee meeting Nov 3, 2022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