U.S. FOOD & DRUG ADMINISTRATION

# Integrated Process and Facilities Assessment

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# Early 2000s: FDA Embarks upon Pharmaceutical Quality for 21st Century Initiative

**Vision**

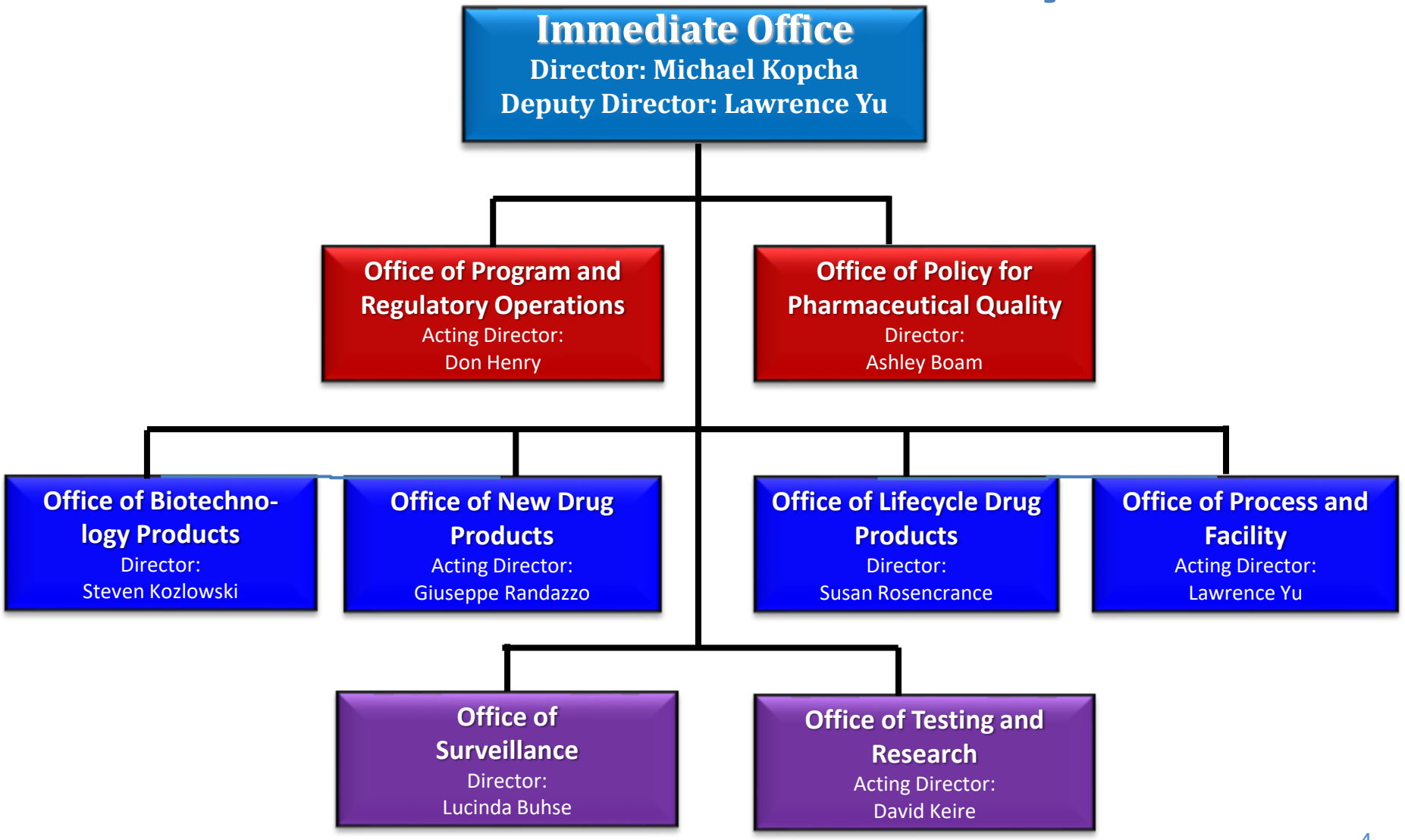
*"A maximally efficient, agile, flexible pharmaceutical manufacturing sector that reliably produces high quality drugs without extensive regulatory oversight."*

**-Dr. Janet Woodcock**

# Office of Pharmaceutical Quality

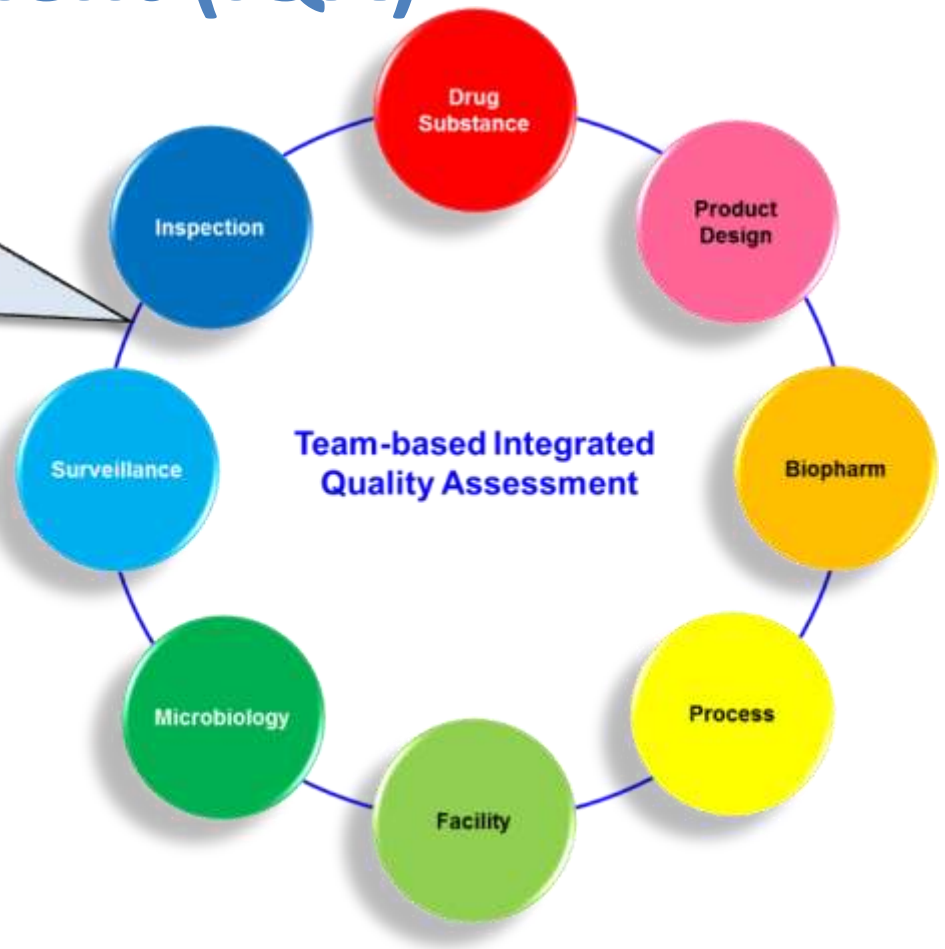
- A single unit dedicated to product quality, across all drug products (new drugs, generics, OTC) and all manufacturing sites (foreign, domestic)
- Alignment of drug quality functions at CDER including assessment, inspection, surveillance, policy, and research
- Integrated quality assessment to streamline regulatory processes, advance regulatory standards, align areas of expertise, and originate surveillance of drug quality

# Office of Pharmaceutical Quality



# Team-based Integrated Quality Assessment (IQA)

Inclusive of drug substance, drug product, manufacturing, and facilities, and maximizes each team member's expertise




**Science- and Risk-Based approach that is patient-focused**

# Team-based Integrated Quality Assessment (IQA)

## The IQA Team


**Application Technical Lead (ATL)** – oversees the scientific content of the assessment
**Business Process Manager (BPM)** – manages the process, adhering to the established timelines

# Mission, Vision, and Core Values of OPF

**Mission**

The Office of Process and Facilities (OPF) ensures that quality is built into manufacturing processes and facilities over the product lifecycle

**Vision**

To be the premier global regulatory organization for holistic assessment of pharmaceutical manufacturing

**Core Values**

- Working as a team, openly sharing knowledge and information in a timely manner
- Partnering with internal and external organizations to achieve "One Quality Voice"

# Facility & Process

- The Process Quality Assessment examines the appropriateness of the design and control strategy of the manufacturing process.
- The Facility Quality Assessment examines the implementation of these controls and evaluates quality systems at the proposed manufacturing facilities.
  - Maintain the control strategy on-site over the life cycle of the product.

*The Process and Facility Reviews are complementary and synergistic. Taken together, these reviews provide a comprehensive assessment of the manufacturing operations proposed in the submission.

# Traditional Process and Facility Assessment

A **Process Quality Assessor** typically:

- Evaluates whether the manufacturing process is understood, developed, and adequately controlled
  - Process and product specific risk factors identified and mitigated
  - Appropriate commercial scale process parameters justified by the development data and scale up strategy
  - Critical in-process controls with specifications
  - Manufacture capability demonstrated by submitted batch records
- Communicates to the applicant through IR comments
- Communicates to the facility reviewer through KTM, emails, T-cons, etc.

# Traditional Process and Facility Assessment (cont.)

A **Facility Quality Assessor** typically

- Evaluates if a Pre-Approval Inspection (PAI) is recommended
  - cGMP compliance history and residual risk of the facility
  - Process and product specific risk in the ANDA
- Participates in PAI (if warranted):
  - Commercial production readiness
  - Conformance with the application
  - Data integrity audit
- Communicates with the inspected facility through on-site dialogue, Form-483 (if issued), RAI Letter, etc.
- Communicates to the process reviewer through emails, T-con, EIR Narrative, etc.

# Integrated Process and Facility Assessment

One (1) **OPF Assessor** will conduct *both* the process and facility quality assessment, and participate in PAI (if warranted):

- Conduct a one time risk assessment on the identified facilities and proposed commercial process, which will increase accuracy and avoid redundancy amongst reviewers
- Determine the need for a PAI after detailed and holistic risk assessment at early stage in the review cycle
- Evaluate process and product risks and mitigations with the knowledge of site cGMP compliance and manufacturing history
- Potential to decrease the occurrence of PAI requests late in the review cycle when additional concerns are found during the Process Assessment
- Streamlines communication between Process and Facility assessments to other members of the review team

# Integrated Process and Facility Assessment (cont.)

Participation of PAI by an OPF Assessor

- Better understanding how the manufacturing process is conducted and controlled, possible reduction of IR comments
- Effective inspection with full knowledge of process and product specific risk
- Real time communication with the applicant with clarity on both the review and inspectional issues
- Possible process and/or facility related corrections/implementations within shorter time frame

# Integrated Process and Facility Assessment
# Case Study 1

Recommendation of a PAI for a Lyophilization drug product at an early review stage

- Process assessment
  - No development data to support the lyo process parameter
  - Inappropriate lyo process parameter
  - Inadequate in-process controls for the lyo process
- Facility assessment
  - Lyophilization not covered during recent inspections
  - Eleven 483 citations related to a similar lyo process issued during a PAI in 2012

# Integrated Process and Facility Assessment
# Case Study 2

Targeted inspection and in time deficiency correction for a modified release tablet

- Review observation: Lack of control for the hole depth during laser drilling
- Inspection observation: Laser power level identified as critical for the hole depth but not monitored and recorded
- Mitigation: Laser power is controlled and P.3 section of the NDA was revised

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