Regulatory Education for Industry (REdI): Pharmaceutical Quality Symposium

Silver Spring, MD | July 20-21, 2016

Greetings!

Online Participants:
Please check your audio volume level.
You should be able to hear music playing.

We will get started at about
8:45 AM Eastern (GMT - 4)


Greenland
Iceland
Canada
United States
Mexico
Venezuela
Colombia
Brazil
Bolivia
Paraguay
Chile
Argentina
Sweden
Norway
Finland
Russia
Ireland
Germany
Poland
Belarus
Ukraine
France
Romania
Italy
Portugal
Turkey
Kazakhstan
Mongolia
Uzbekistan
Turkmenistan
Afghanistan
Iran
Iraq
Syria
Saudi Arabia
Egypt
Libya
Algeria
Morocco
Mali
Niger
Chad
Sudan
Nigeria
South Sudan
Ethiopia
Somalia
Kenya
DR Congo
Tanzania
Angola
Zambia
Mozambique
Zimbabwe
Namibia
Botswana
South Africa
Madagascar
China
India
Myanmar
Thailand
Malaysia
Indonesia
Philippines
Australia
Papua New Guinea

Regulatory Education for Industry (REdI): Pharmaceutical Quality Symposium

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Welcome!

Capt. Brenda Stodart, PharmD

Program Director, CDER Small Business & Industry Assistance

Division of Drug Information

Office of Communications

CDER, FDA

FDA's Office of Pharmaceutical Quality (OPQ)
An Overview and Update

Michael Kopcha, Ph.D., R.Ph.
Director
Office of Pharmaceutical Quality
CDER/FDA

Regulatory Education for Industry (REdI) - Pharmaceutical Quality Symposium
July 20, 2016

Outline

- Overview/Design of OPQ
- OPQ Accomplishments in 2015
- OPQ 2016 Priorities
- The Partnership of FDA and Industry

Overview/Design of OPQ

Office of Pharmaceutical Quality (OPQ)

Mission

The Office of Pharmaceutical Quality assures that quality medicines are available to the American public

Vision

The Office of Pharmaceutical Quality will be a global benchmark for regulation of pharmaceutical quality

Slogan

'One Quality Voice'

'One Quality Voice' Value Statements

- **Put patients first** by balancing risk and availability
- Have one quality voice by **integrating review and inspection** across product lifecycle
- Safeguard clinical performance by establishing **scientifically sound quality standards**

'One Quality Voice' Value Statements

- Maximize focus and efficiency by applying **risk-based approaches**
- Strengthen the effectiveness of lifecycle quality evaluations by using **team-based processes**
- Enhance quality regulation by developing and utilizing staff expertise

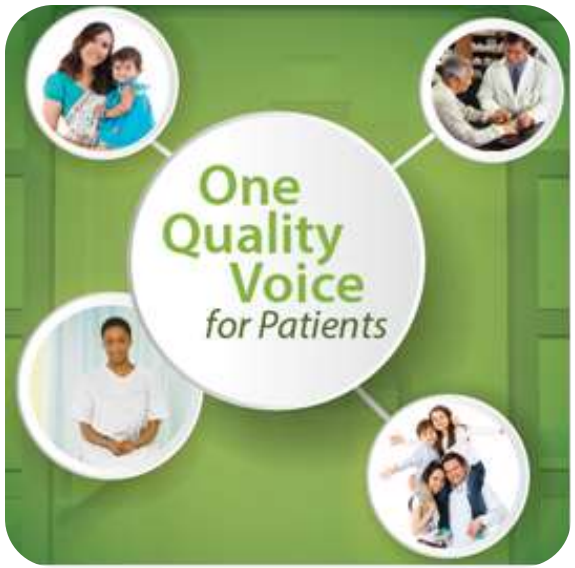
'One Quality Voice' Value Statements

- Encourage innovation by advancing **new technology and manufacturing science**
- Provide effective leadership by emphasizing cross-disciplinary interaction, shared accountability, and joint problem solving
- Build **collaborative relationships** by communicating openly, honestly, and directly

Objectives of OPQ

- A single unit in CDER dedicated to drug product quality that fosters close integration of major functional areas

Objectives of OPQ



- Implement a lifecycle approach to quality that spans pre- and post-approval for both brand and generic drugs

Objectives of OPQ

- Balance potential quality risks with the risk of a patient not getting a drug
- Anticipate quality problems before they develop to help prevent drug shortages

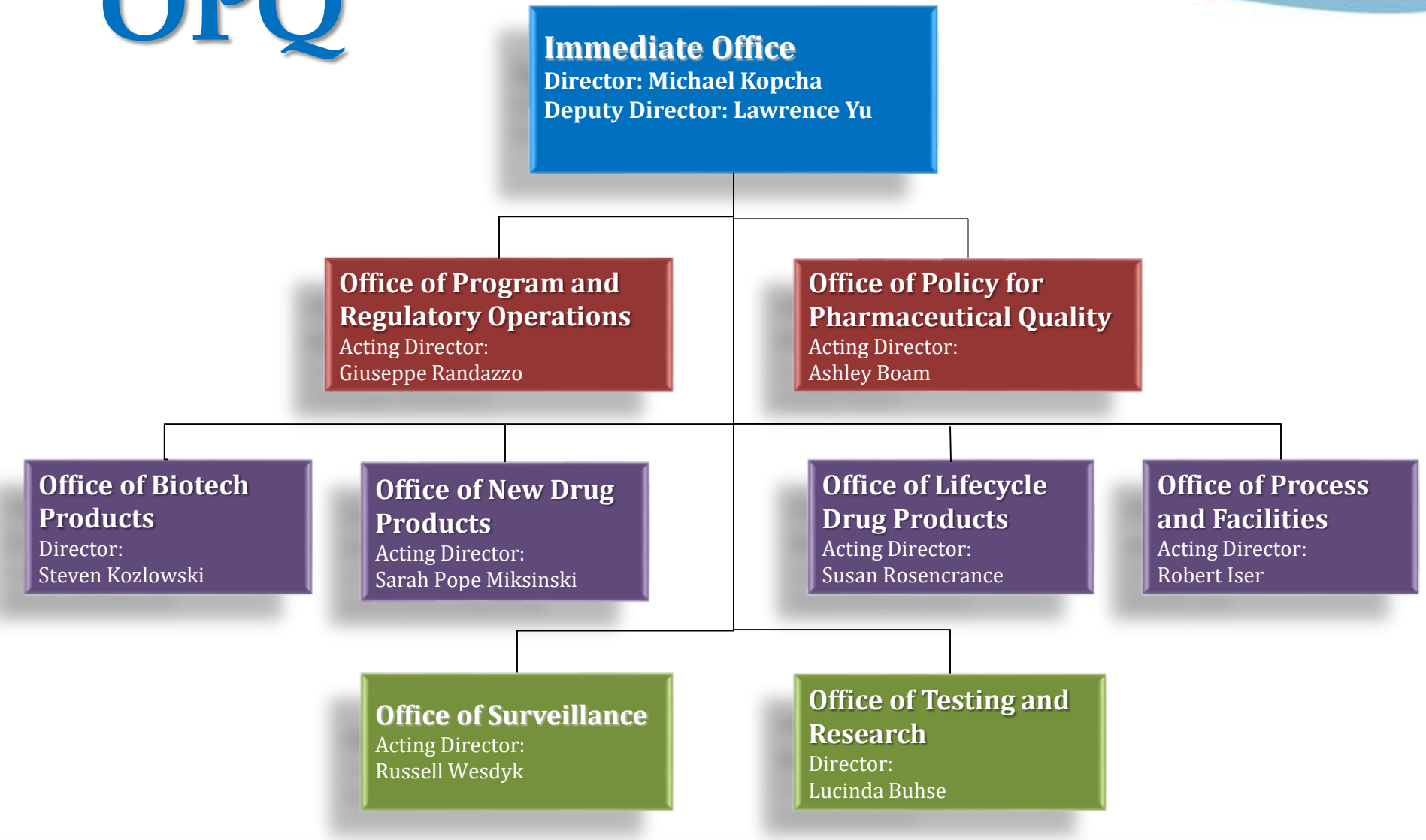
Objectives of OPQ

- Establish consistent, clinically relevant quality standards and clear expectations for industry
- Emphasize quality metrics and surveillance techniques to help monitor quality across facilities
- Encourage use of modern, more efficient manufacturing technologies

OPQ

- To keep pace with increasing product complexity, OPQ is organized based on discipline and expertise
- The review function matrices across OPQ for enhanced interactions, communication, and consistency among sub-offices
- Functional areas align for the purpose of streamlining FDA processes that monitor drug quality

OPQ


Immediate Office
Director: Michael Kopcha
Deputy Director: Lawrence Yu
Office of Program and Regulatory Operations
Acting Director:
Giuseppe Randazzo
Office of Policy for Pharmaceutical Quality
Acting Director:
Ashley Boam
Office of Biotech Products
Director:
Steven Kozlowski
Office of New Drug Products
Acting Director:
Sarah Pope Miksinski
Office of Lifecycle Drug Products
Acting Director:
Susan Rosencrance
Office of Process and Facilities
Acting Director:
Robert Iser
Office of Surveillance
Acting Director:
Russell Wesdyk
Office of Testing and Research
Director:
Lucinda Buhse

Office of Program and Regulatory Operations
Acting Director:
Giuseppe Randazzo

– Office of Program and Regulatory Operations (OPRO)

- Manages the business processes associated with drug product quality assessment and facility inspections
- Facilitates a quality management system
- Handles learning and professional development programs

Office of Policy for Pharmaceutical Quality
Acting Director:
Ashley Boam

– Office of Policy for Pharmaceutical Quality (OPPQ)

- Develops, implements, and updates science- and risk-based policies, standards, and guidance documents related to drug product quality and assessment
- Ensures consistent interpretation and application of drug product quality policies and programs

Office of Biotech Products
Director:
Steven Kozlowski

Office of New Drug Products
Acting Director:
Sarah Pope Miksinski

Office of Lifecycle Drug Products
Acting Director:
Susan Rosencrance

- **Office of Biotechnology Products (OBP), Office of New Drug Products (ONDP), and Office of Lifecycle Drug Products (OLDP)**
  - Perform quality assessment of the drug substance, drug product, and biopharmaceutics portions of applications (NDAs, ANDAs, BLAs, and supplements)
    - Formulation/product design
    - Risk assessment
    - Quality standards and clinically relevant specifications
    - Control strategy related to product attributes
    - Stability

Office of Process and Facilities
Acting Director:
Robert Iser

– Office of Process and Facilities (OPF)

- Performs quality assessment of the manufacturing process for applications (NDAs, ANDAs, BLAs, and complex supplements)
  - Ensures successful implementation of manufacture at commercial scale
  - Advises on applied microbiological issues related to product quality and manufacture
  - Advises on inspectional and facility issues related to applications

Office of Surveillance
Acting Director:
Russell Wesdyk

– Office of Surveillance (OS)

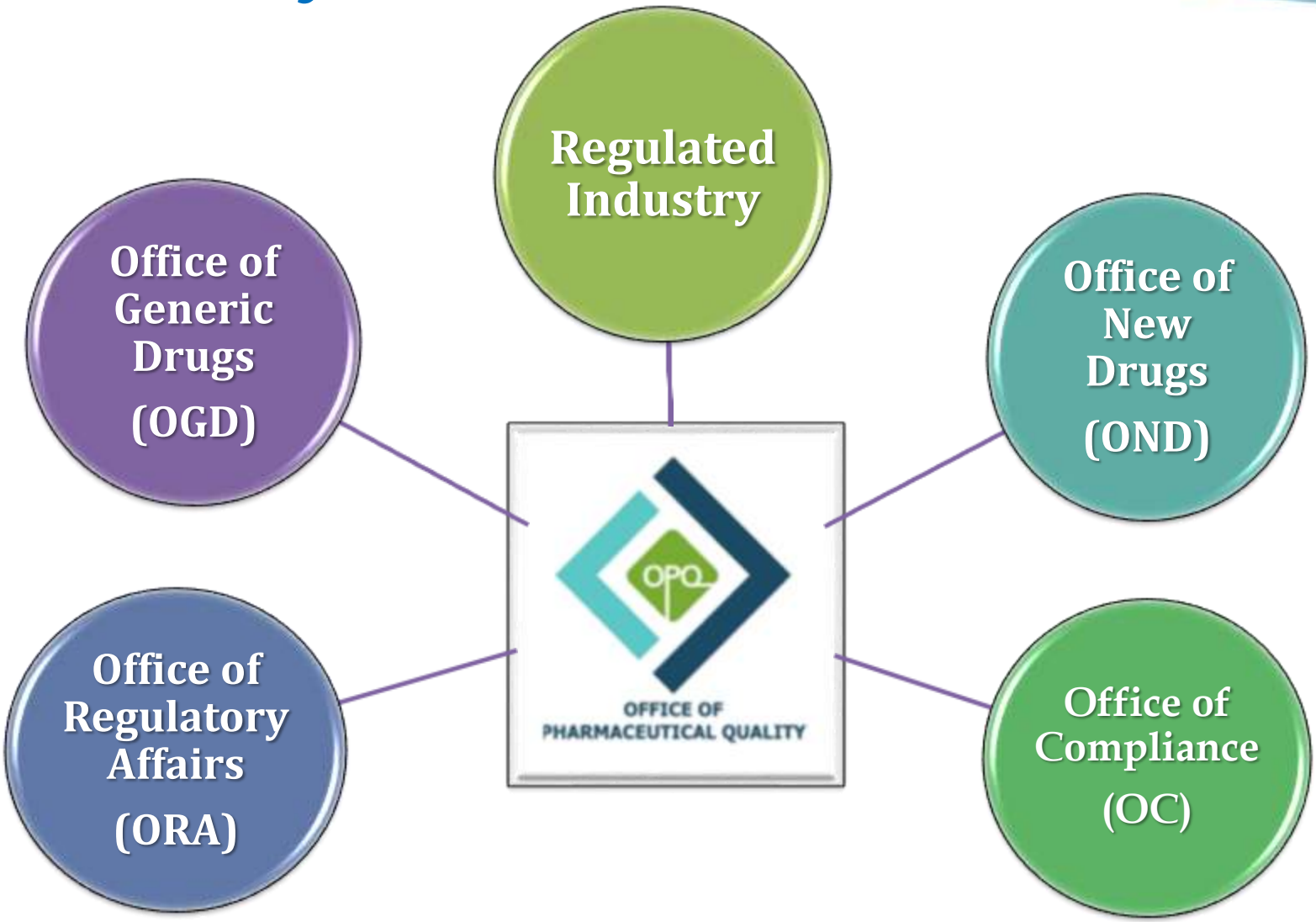
- Monitors quality and manages information about the entire inventory of CDER-regulated sites and products
  - Generates and manages knowledge related to the 'state of quality' for both facility and product using a set of quality metrics
  - Intelligence generated strengthens ability to make risk-based decisions that govern inspection frequency and coverage
  - Allows for rapid response to process trends before serious quality problems occur

Office of Testing and Research
Director:
Lucinda Buhse

– Office of Testing and Research (OTR)

- Performs research on the manufacture, formulation, and characterization of drug products that supports the development of scientific standards and policies
  - Collaborates with the review and policy offices to help advance science and establish standards related to quality, especially for complex products
- Directs drug product quality surveillance testing and laboratory-based investigational activities.

OPQ's Key Stakeholders



OPQ Accomplishments in 2015

OPQ Accomplishments - 2015

- OPQ is responsible for meeting program performance goals under the:
  1. Generic Drug User Fee Amendment (GDUFA)
  2. Prescription Drug User Fee Act (PDUFA); and
  3. Biosimilar User Fee Act (BsUFA)

- In 2015 all performance goals were met or exceeded in each program area

OPQ Accomplishments - 2015

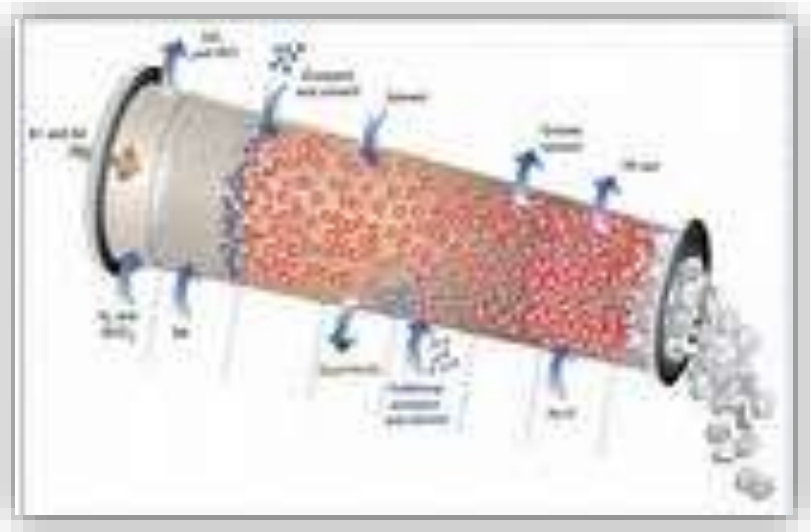
- Played a critical role in the following high-profile CDER approvals

  1. First generic version of Copaxone (glatiramer acetate injection) used to treat patients with relapsing forms of multiple sclerosis (MS)

  2. First biosimilar product – Zarxio (filgrastim-sndz) for the treatment of neutropenia associated with chemotherapy

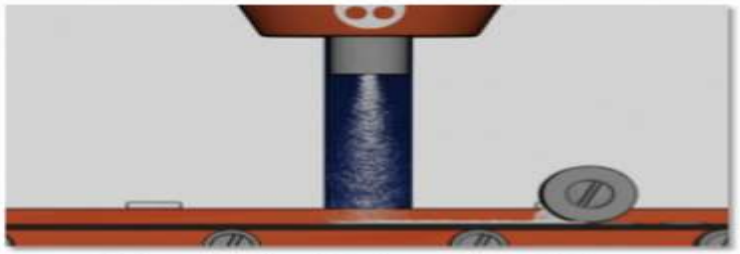
OPQ Accomplishments – 2015

3. First continuous manufacturing process
   - Orkambi, a combination therapy for treatment of cystic fibrosis (CF)

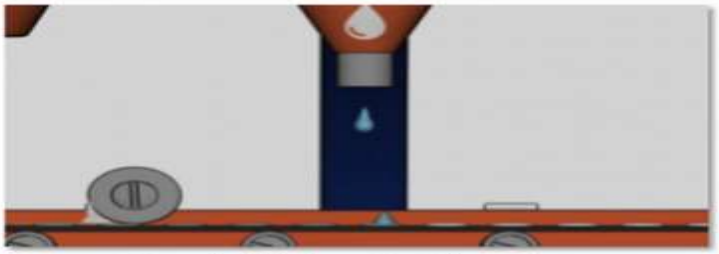


OPQ Accomplishments - 2015

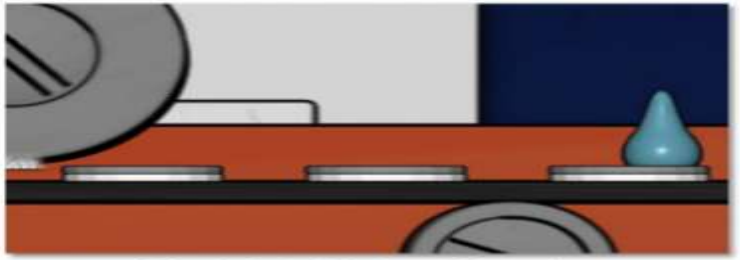
4. First 3D-printed drug product – Spritam
   - A groundbreaking technique that uses three-dimensional printing to produce a porous formulation that rapidly dissolves with a sip of water



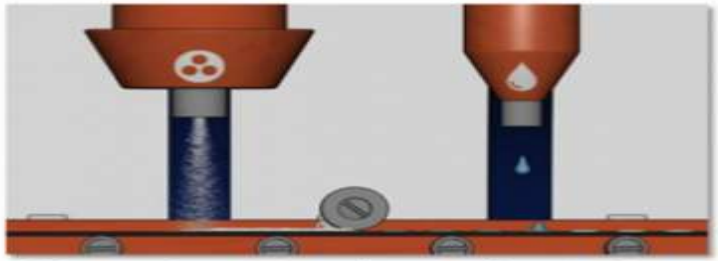
First, a powdered medicine is spread into a thin layer.



Then, a liquid is dropped onto the powder.



This selectively binds the particles together in a thin, porous layer.



This process is repeated a specific number of times to add more layers based on the dosage, building the product from bottom to top.

OPQ 2016 Priorities

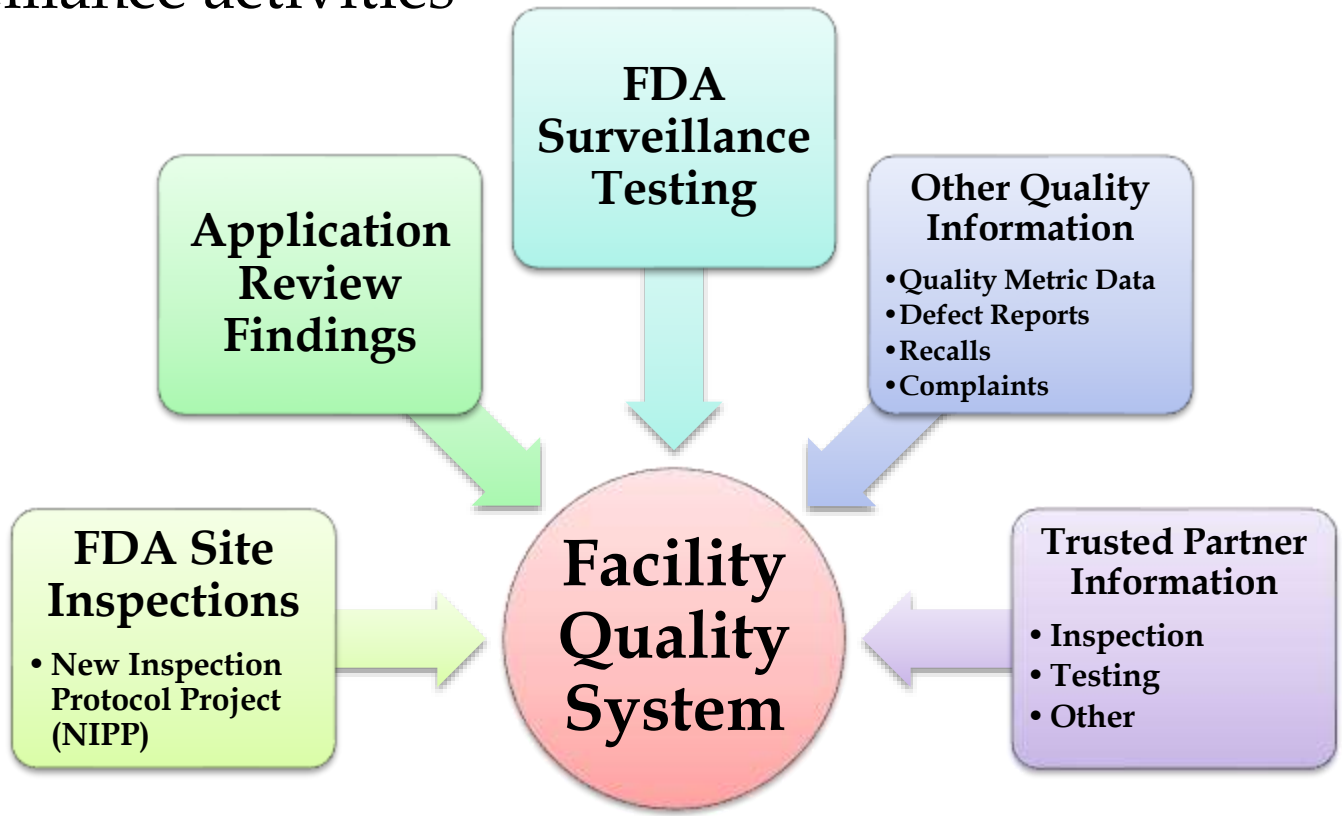
I. Facility Assessments/Inspections

OPQ Priority: A more rigorous and comprehensive approach to drug quality surveillance and inspection

- **Quality Metrics** to better monitor the current status of product and facility across the inventory of FDA-regulated sites and inform FDA risk-based surveillance inspection planning
- **New Inspection Protocol Project (NIPP)** – Provides a more quality-focused, semi-quantitative approach to inspections with more streamlined and structured reporting

I. Facility Assessments/Inspections

- **Common Informatics Platform** that integrates the knowledge captured during review, inspection, and surveillance activities



II. Team-based Integrated Quality Assessment (IQA)

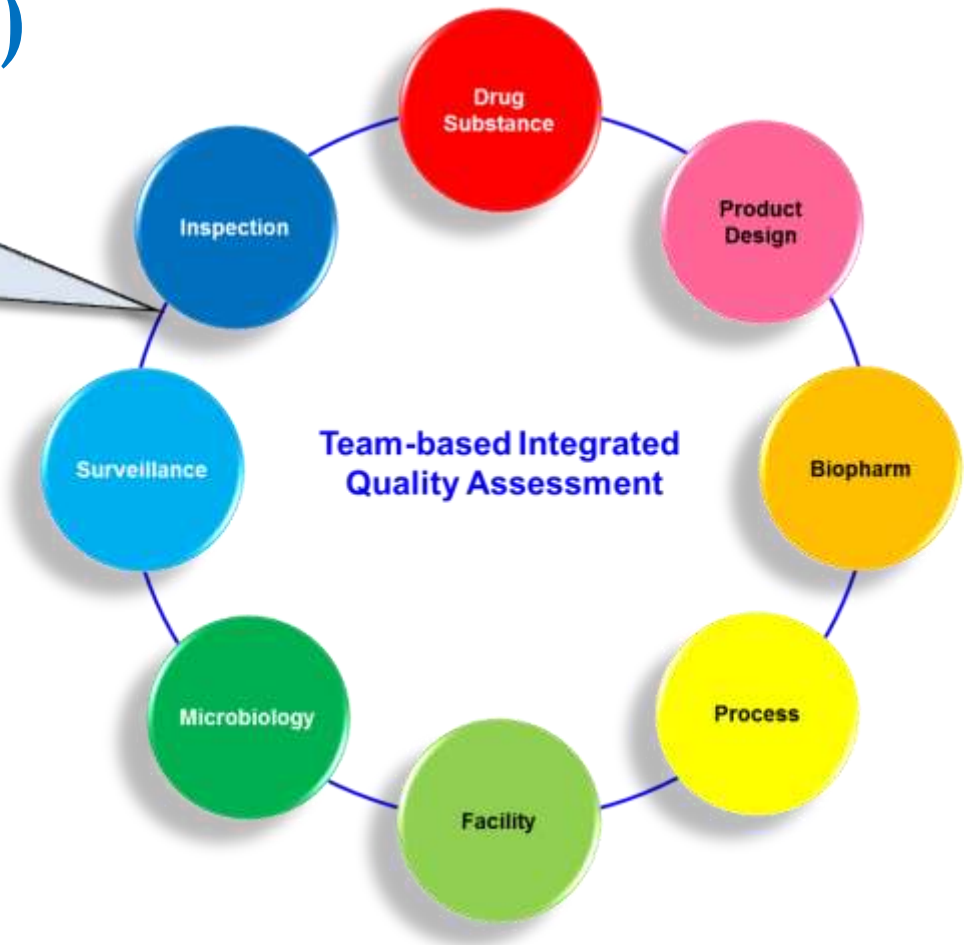
OPQ Priority: Quality assessments of ANDAs, NDAs, and BLAs that effectively align patient-focused and risk-based recommendations

- A team of subject-matter experts performing a quality assessment of an application (ANDA, NDA, BLA) based on risk and knowledge management
- This approach is on-going for all original ANDAs*, NDAs, and BLAs

* ANDAs submitted after October 1, 2014

II. 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

II. Team-based Integrated Quality Assessment (IQA)

The IQA Review Team

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

II. Team-based Integrated Quality Assessment (IQA) - Advantages

- Close collaboration and communication among disciplines in a team environment yields better decision making
- Assures the application of uniform quality standards and promotes consistent regulatory practices for both brand and generic drug products

II. Team-based Integrated Quality Assessment (IQA) - Advantages

- Integration of quality review with inspection results in more informed decision making on facility acceptability and application approvability

II. Team-based Integrated Quality Assessment (IQA) - Advantages

- Promotes building an integrated knowledge base that allows for:
  - Clear identification of product risks
  - Quickly addressing quality problems
  - Improving overall efficiency and effectiveness in managing the drug product lifecycle

II. Team-based Integrated Quality Assessment (IQA) - Advantages

- Knowledge about quality issues gained from the review of the brand product can be appropriately applied to the review of the generic product

III. Risk Management and Communication

OPQ Priority: Formal risk-based regulatory approaches that effectively define the scope and extent of quality assessments

- Currently OPQ employs a formal risk assessment process to best allocate resources based on product risk and patient impact
  - Maintaining structured risk assessments that focus on product failure modes and specific risks to patients
  - Developing use of the structured risk assessment as a communication tool with investigators and reviewers for more informed decision making, knowledge transfer, and good lifecycle management

III. Risk Management and Communication

- **The Desired Future State** – A unified risk evaluation for brand and generic products that integrates the structured risk assessment with the existing drug product knowledge base
  - Provides a risk profile and ranking of a drug product's critical quality attributes (CQAs) during the pre-marketing phase
  - May also include information on the manufacturing site and quality system
  - Utilized in the post-marketing phase to assess proposed changes and the associated risks to product quality
  - Provides a comprehensive summary of the current state of quality for all approved NDAs/ANDAs of a particular drug product
  - Unique for each drug product and each manufacturer potentially allowing for individualized regulatory oversight of post-approval changes

III. Risk Management and Communication

RISK RATING TABLE

IMPACT					
5	M	H	H	H	H
4	M	M	H	H	H
3	L	L	M	M	H
2	L	L	L	L	M
1	L	L	L	L	L
	1	2	3	4	5

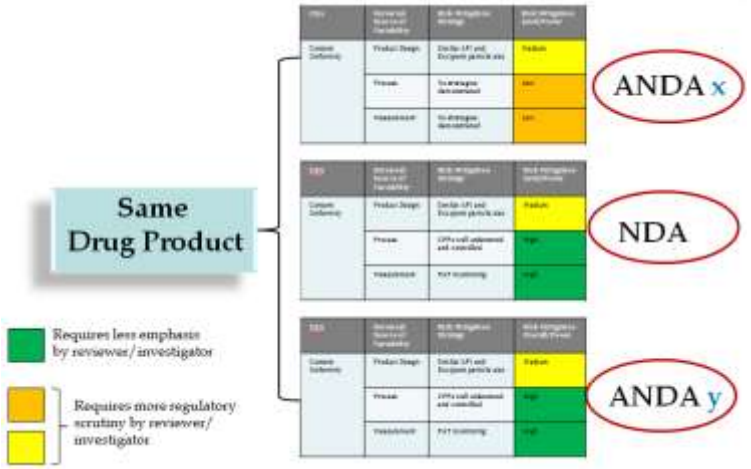
LIKELIHOOD

H = High Risk
M = Moderate Risk
L = Low Risk

Past:
Informal risk assessment

Now: Formal risk assessment for individual applications

Future: Drug Product Dashboard



IV. Emerging Technology

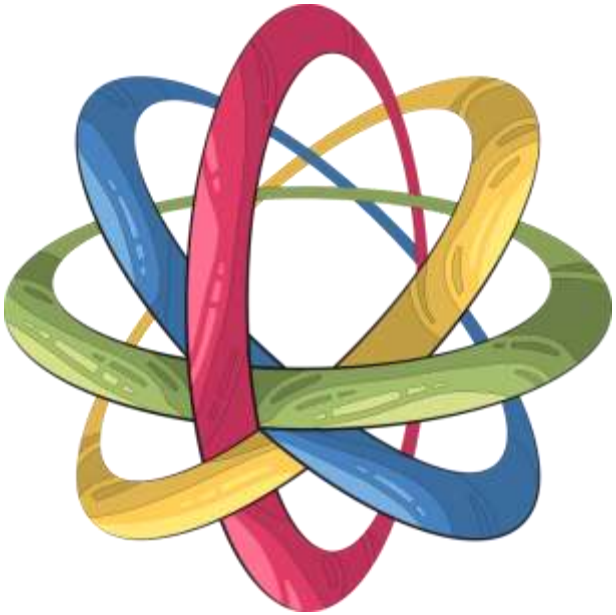
OPQ Priority: A collaborative approach with manufacturers that encourages innovation and the adoption of new technologies

- The Emerging Technology Team (ETT) within OPQ:
  - Serves as a centralized location for external inquiries on emerging technology
  - Provides a forum for early dialogue with FDA
  - Ensures consistency, continuity, and predictability in review and inspection of new technologies
  - Participates in the team-based integrated quality assessment when new technologies are evaluated

IV. Emerging Technology

- The Emerging Technology Team (ETT) has been actively working on topics such as continuous manufacturing, 3D-printing drug products, novel aseptic filling technology, and new container/closure systems

- Generic manufacturers are encouraged to consider these advanced technologies – we will work with you!



The Partnership of FDA and Industry

Our Common Goal is Drug Product Quality

- OPQ aligns and integrates all quality functions within CDER marking a new era in FDA's quality oversight.

- Let us communicate, collaborate, and work together to deliver a high quality product that meets the patient's needs – a true partnership!

Working in true partnership we will achieve the vision

The Vision

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

-Dr. Janet Woodcock

Thank you!