State of Office of Pharmaceutical Quality (OPQ) Address

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Outline

- OPQ Mission, Vision, and Strategic Priorities
- OPQ Organization Updates
- UFA updates as it relates to OPQ
- OPQ Sub-Office snapshots and operational requests
- Closing Remarks

OPQ Mission, Vision, and Strategic Priorities

Office of Pharmaceutical Quality

Pharmaceutical quality is our *shared* goal of seeing consistently safe and effective drugs 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

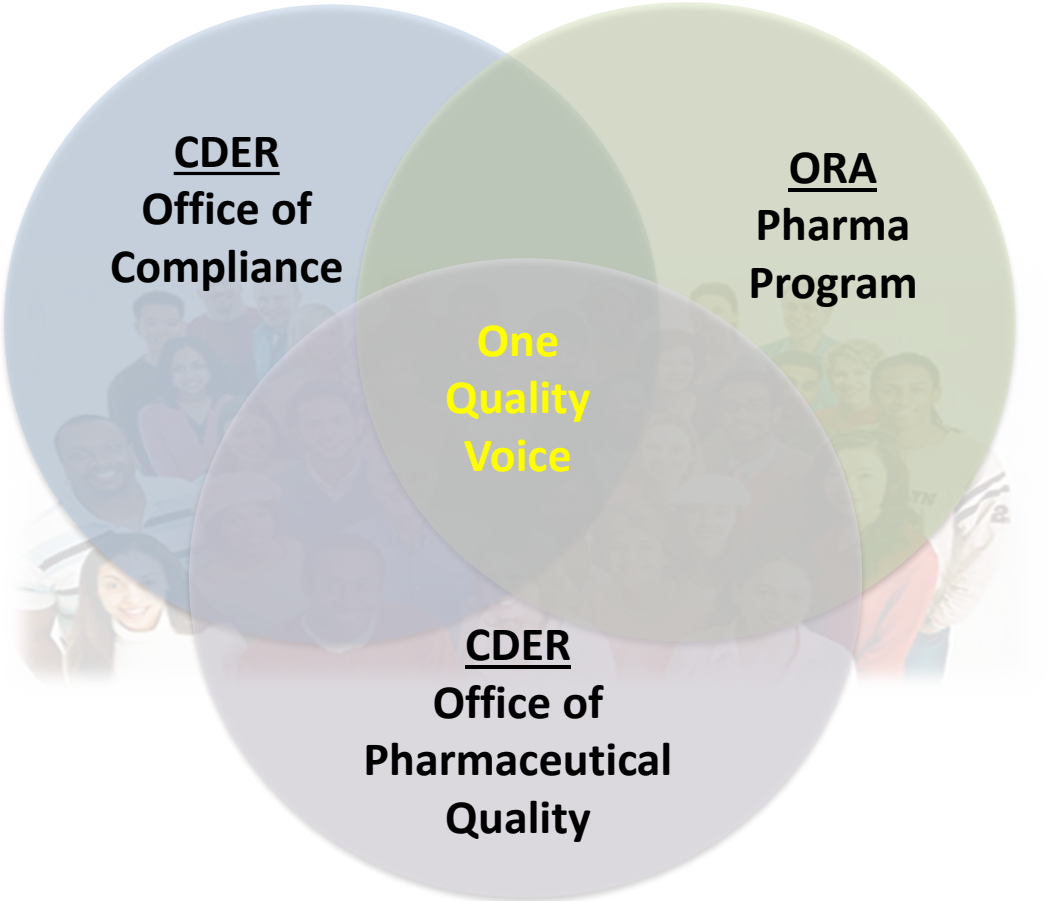
Vision

OPQ will be a global benchmark for regulation of pharmaceutical quality

Motto

‘One Quality Voice’

One Quality Voice



Office of Pharmaceutical Quality

- To keep pace with increasing product complexity, OPQ is organized around discipline and expertise
- The review function matrices across OPQ allow for enhanced interactions, communication, and consistency among sub-offices
- Functional areas align to streamline FDA processes that assess and monitor drug quality

OPQ Strategic Priorities: FY 2018

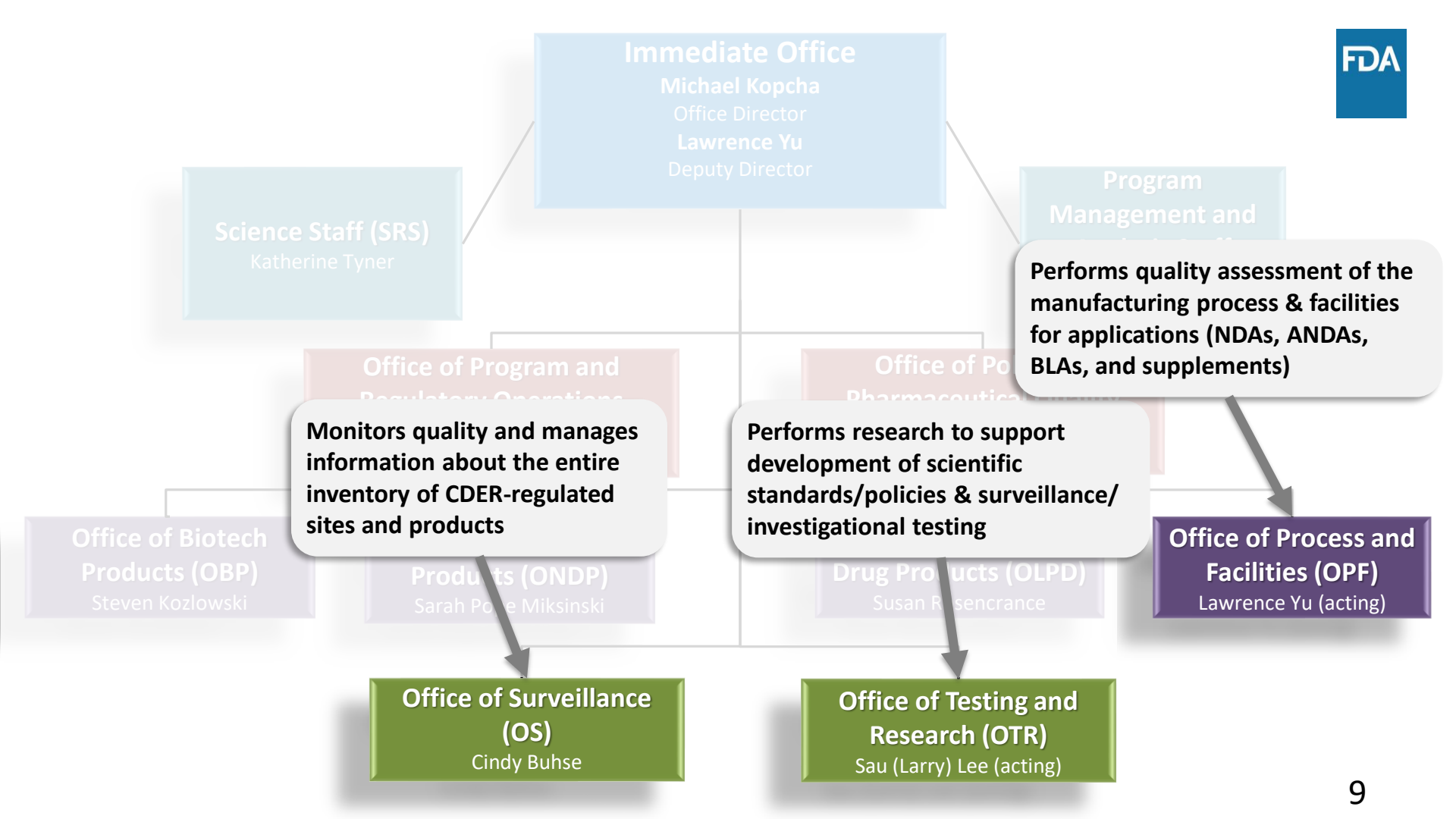
1. **Strengthen OPQ's collaborative organization**
   - Leverage a collaborative culture, an engaged and empowered workforce, streamlined processes, and effective teaming to ensure an efficient, high-performing, innovative, and results-oriented organization

2. **Promote availability of better medicines**
   - Minimize barriers to encourage innovation within FDA and in the manufacturing sector through sensible oversight, research, risk-based decision-making, and continuous process improvement

3. **Elevate awareness and commitment to the importance of pharmaceutical quality**
   - Effectively communicate the importance of quality and that the American public can trust their drugs

4. **Strengthen partnerships and engage stakeholders**
   - Build productive relationships with business partners within and outside FDA and jointly foster effective stakeholder engagement to meet the needs of the American public

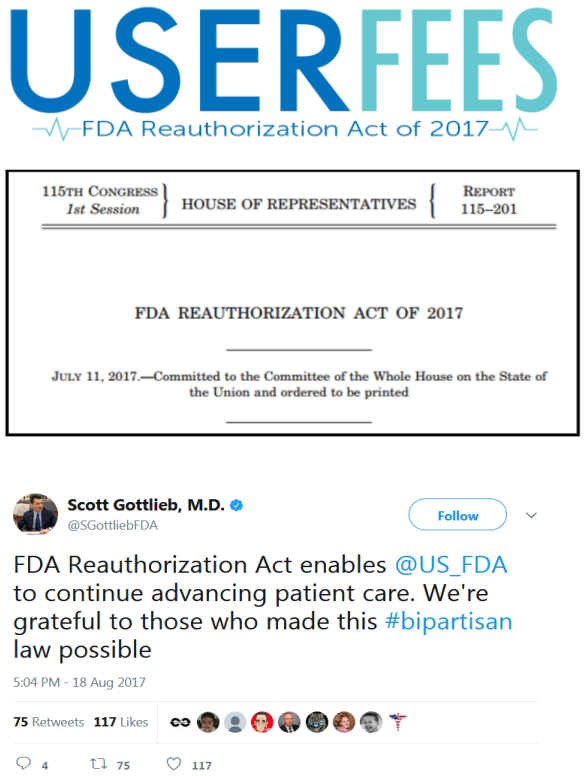
OPQ Organization Updates


Immediate Office
Michael Kopcha
Office Director
Lawrence Yu
Deputy Director
Science Staff (SRS)
Katherine Tyner
Program Management and
Performs quality assessment of the manufacturing process & facilities for applications (NDAs, ANDAs, BLAs, and supplements)
Office of Program and
Monitors quality and manages information about the entire inventory of CDER-regulated sites and products
Performs research to support development of scientific standards/policies & surveillance/ investigational testing
Office of Biotech Products (OBP)
Steven Kozlowski
Office of Process and Facilities (OPF)
Lawrence Yu (acting)
Office of Surveillance (OS)
Cindy Buhse
Office of Testing and Research (OTR)
Sau (Larry) Lee (acting)

UFA updates as related to OPQ

Quality Changes Related to the UFAs

- FDA Reauthorization Act, signed into law 8/18/17, reauthorizes:
  - The Generic Drug User Fee Amendments (GDUFA) for the first time
  - The Prescription Drug User Fee Act (PDUFA) for the fifth time
  - The Biosimilar User Fee Act (BsUFA) for the first time
- User fees provide critical resources to conduct product assessments in a timely fashion and help ensure the quality, safety, and effectiveness of drug products
- The new UFAs bring some changes impacting our quality assessment, some more significant than others



Quality Changes Related to GDUFA

GDUFA II

- All original ANDAs and ANDA amendments fall within a single assessment scheme (90% goals)
- Creation of a new pre-ANDA program for complex products
  - Product development, pre-submission and mid-cycle meetings for complex ANDAs
- Creation of new GDUFA II deliverables (e.g., DRLs)
- Restructuring of the user fee program to provide resources commensurate with the workload

Standard Original	• **10 months (mths)**
Priority Original	• **8 mths w/ PFC*** • **10 mths w/o PFC**
Standard Major Amendment	• **8 mths w/o inspection** • **10 mths w/ inspection**
Priority Major Amendment	• **6 mths w/o inspection** • **8 mths w/ inspection & PFC unchanged** • **10 mths w/ inspection & no/changed PFC**
Standard/Priority Minor Amendment	• **3 mths**

***Presubmission Facility Correspondence (PFC)** lists all facilities for manufacturing (including labs, etc.) with confirmation the facility is ready for inspection, plus sites for BE/clinical studies

Quality Changes Related to BsUFA

BsUFA II

- Assess 90% of applications within 10 months of the *60-day filing date*
  - Date when an applicant is notified if the application has been accepted by FDA for assessment
  - BsUFA I was within 10 months of *receipt*
- 60 days allows for additional communications and interactions between FDA assessment teams and biosimilar applicants
- Establishes an assessment model similar to “the Program” for new drugs
  - Promotes the first cycle assessment process
  - Minimizes the number of assessment cycles
- If there is a need to inspect a facility that was not included on the list of facilities, the FDA may extend the goal date, consistent with PDUFA VI
- Fee structure is more reflective of workload and resources needs for BsUFA
  - Financial predictability and transparency

OPQ Sub-Office snapshots … and operational requests

OPPQ: Quality Policy in 2017

- Published **7 MAPP documents**
- Responded to **220 external inquiries**
- Responded to **371 controlled correspondence**
- Published **7 guidance documents**
  - ANDAs: Pre-Submission of Facility Information Related to Prioritized Generic Drug Applications
  - Advancement of Emerging Technology Applications for Pharmaceutical Innovation and Modernization (Final)
  - CMC Post-approval Manufacturing Changes for Specified Biological Products To Be Documented in Annual Reports
  - Expiration Dating of Unit-Dose Repackaged Solid Oral Dosage Form Drug Products
  - Child-Resistant Packaging Statements in Drug Product Labeling
  - Current Good Manufacturing Practice for Medical Gases
  - Extending Expiration Dates of Doxycycline Tablets and Capsules in Strategic Stockpiles

OS: New Inspection Protocol Project (NIPP)

- In 2016-2017, in collaboration with ORA and OC, OPQ:
  - Completed pilot inspections (surveillance and pre-approval) for sterile drug process facilities.
  - Based on feedback from pilots, improved the inspections protocols.
  - Prepared for another set of pilot inspections in FY2018. Developed a workplan for implementation of NIPP for sterile drug process facilities and other dosage forms.

OPF: OPQ/ORA working better together

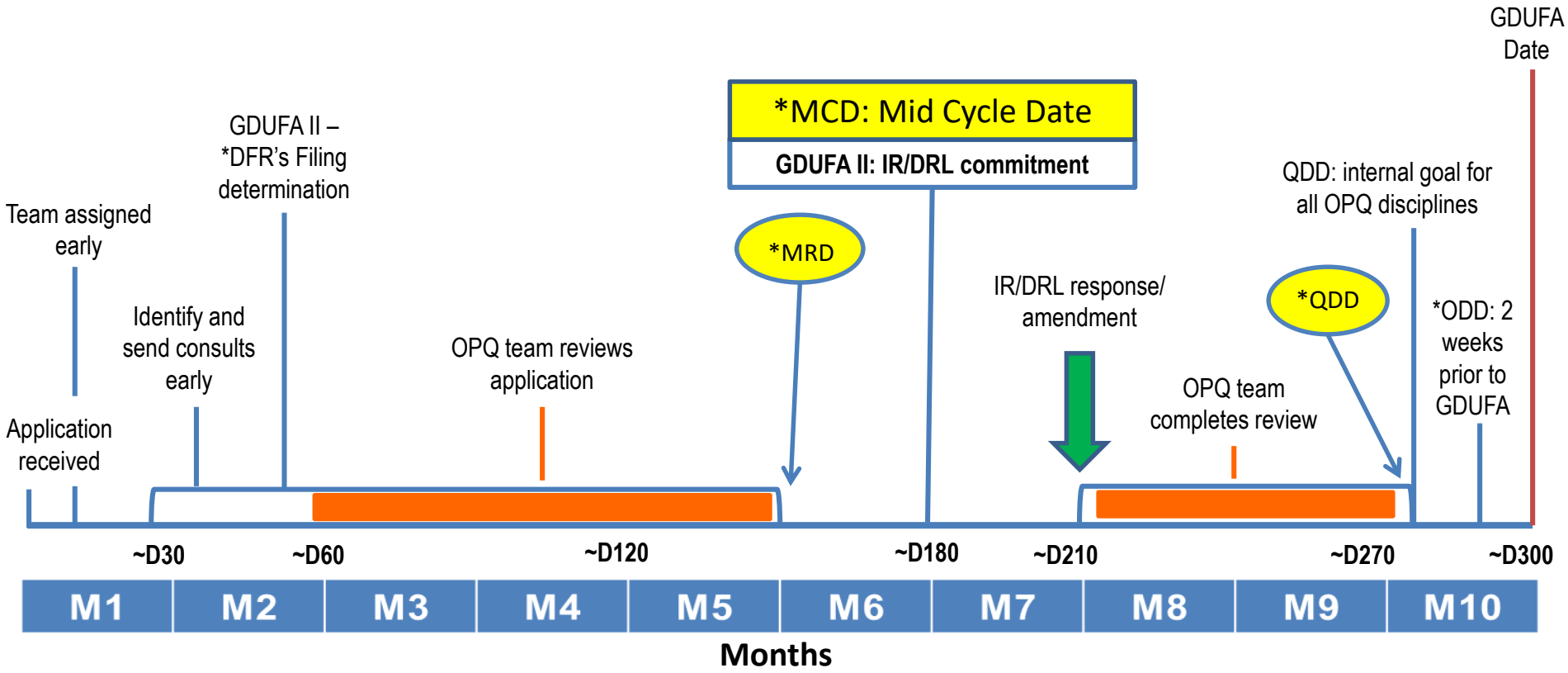
- Concept of Operations signed in Summer 2017, a collaboration between ORA, OC, and OPQ
  - Outlines the workflow processes for **Pre-Approval**, **Post-Approval**, **Surveillance**, and **For-Cause** Inspections
  - Defined and clarified the roles and responsibilities of CDER and ORA
- Ensures **consistency, efficiency, and transparency** in facility evaluations, inspections, and regulatory decision-making for marketing applications
- Improves **strategic alignment** and **operational capacity** by enhancing collaboration across CDER and ORA

ONDP: Biopharmaceutics: Clinical Relevance

- QC in vitro release testing (e.g. dissolution) should ensure release of product that maintains clinical performance (i.e. bioequivalence)
- Attempts should be made to adhere to recommendations as outlined in the 2015 draft guidance "*Dissolution Testing and Specification Criteria for Immediate-Release Solid Oral Dosage Forms Containing Biopharmaceutics Classification System Class 1 and 3 Drugs*"
- Justifications can be provided (e.g. in silico modeling, literature) to ensure that quality specifications are able to detect changes that affect BE

https://www.fda.gov/downloads/Drugs/Guidances/UCM456594.pdf

GDUFA II snapshot of OPQ process timeline – 10 month example for Original ANDAs



*DFR = OGD's Division of Filing Review; MRD = Mid Review Date;
MCD = Mid Cycle Date; QDD = quality Due date; ODD = owner due date

ONDP (DMF): Drug Substance Review

- Cohort year 2018 ANDAs are now assigned so that the DMF review is aligned with DP review and assessment review team to meet “mid-cycle” milestones.
- DMF staff checking early in the review clock for potentially needed facilities to be listed in the application (early IR)
- First Adequate Letters are now issued to DMF holders when the DMF is adequate for the first time. DMF holders should use this information to avoid submitting unsolicited amendments late in the ANDA review clock.
- Guidance development for Post Approval Changes for drug substances is on track to meet the October 1, 2018 draft issuance date.

OPRO/OLDP: Key consideration and requests

- Accuracy and transparency on FDA forms and cover letters
  - Form FDA 356h to be completed accurately
  - Cover letter: be specific, reference FDA/Industry communications and … tell the story!
  - Industry responses to FDA
    - Complete
    - Substantive
    - Timely
  - Industry to improve communications with their working partners (e.g. DMF and CMOs)

OPRO/OLDP: FAQs during internal training

- Q: Can we send an IR prior to the DRL? A: Yes
- Translation to industry:
  - You may receive an IR prior to the DRL for GDUFA II applications. (These could be in the form of single discipline or consolidated.)

- Q: Can applicants partially respond to DRLs? A:
  - OPQ expectation and recommendation is to have industry fully respond to the DRL by addressing ALL "possible deficiencies" wholly and with a singular complete submission
  - Partial responses, will likely be the exception rather than the rule, but is permitted on a case-by-case basis
  - Contact your RBPM to discuss why you may not be able to address your DRL with one complete submission and we will work with you on appropriate steps forward

Closing Remarks

- Connecting the NOW (the operational framework) into our long term strategy
- Working internally together in addition to working with industry, patients, trades, and others to continuously improve for the sake of the American public.
- **We all have a shared responsibility! As we continue to focus on patients and consumers, together we can provide them confidence in their *next* dose.**

Thank you!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ADMINISTRATION

Backup slides

Quality Changes Related to PDUFA

PDUFA VI

- Current practices regarding Program flexibility for expedited assessments are now part of PDUFA VI
- Advisory Committee Meetings will be no later than 2 months ~~3 months~~ (standard) or no later than 6 weeks ~~2 months~~ (priority) prior to the goal date
- Discipline Review Letters are no longer part of the performance under PDUFA VI
- All original applications and supplements are expected to include a comprehensive and readily located list of ALL manufacturing facilities
- If there is a need to inspect a facility that was not included on the list, FDA may extend the goal date
  - **3 months** for an original application or efficacy supplement
  - **2 months** for a manufacturing supplement
  - Only one extension permitted per assessment cycle (e.g., either major amendment clock extension or facilities clock extension)