PEPFAR
U.S. President's Emergency Plan for AIDS Relief

U.S. FOOD & DRUG ADMINISTRATION

Drug Product Quality Assessment Considerations Under PEPFAR

Presented by: **Peter Capella, PhD**
Division Director,
DIMRPII/OLDP/OPQ/CDER/FDA

Drug Product Quality Assessment Considerations Under PEPFAR

Overview –

- Differences in Standards between US Drug Product and PEPFAR Drug Product Quality Assessments (DPQAs)
- Overcoming the early challenges to performing PEPFAR DPQAs
- How assessment practices have evolved during the PEPFAR *and* GDUFA*
- Current areas of focus for PEPFAR both pre- and post-Tentative Approval

{* Generic Drug User Fee Acts; 2012, 2017, *2022}*

A ***Quick View*** of Drug Product Quality Considerations for all FDA-Approved Drugs for the US Market

Patient-centric (Our focus is always on benefit/risk to the patients)

- Looking for Acceptable and Reproducible Drug Product Quality

- Submission Requirements for Assessment of Drug Product Quality
    - Demonstration of Product Knowledge and Understanding (K&U)
        - Data Provided to Support that K&U
            - Raw Materials, Processes, and Facilities
            - Batch Release, Stability Studies and Validated Methods

Drug Product Quality considerations for **PEPFAR** FDA Tentatively-Approved Drugs

Patient-Centric (Our focus is always benefit/risk to the patients)

- Looking for Acceptable and Reproducible Drug Product Quality

- Submission Requirements for Assessment of Drug Product Quality
  - Demonstration of Product Knowledge and Understanding
    - Data Provided to Support that Knowledge and Understanding
      - Raw Materials, Processes, and Facilities
      - Batch Release, Stability Studies and Validated Methods

One Specific Difference in Drug Product Quality considerations for PEPFAR FDA Tentatively-Approved Drugs vs. FDA Approved Drug for the US Market

DP Storage Temperatures:

USA: ICH Zones I and II (25°C/60%RH)
PEPFAR: ICH Zones III and IV (30°C/75%RH)

NOTE: We (FDA) need assurance that product quality will be maintained for the medicine under storage conditions that the medicine will encounter in the patient's home.

Challenges for Drug Product Quality Assessments PEPFAR Drugs during early days of PEPFAR

Time Constraints

Urgency in Early Days was Severe due to Minimal Number of Medications Available

FDA Resource Constraints

Limited Scientific Staff Prior to GDUFA;
The Single Scientist Assessment Approach

How FDA overcame these challenges for Drug Product Quality Assessments Drugs

Time Constraints

Urgency in Early Days was Severe due to Minimal Number of Medications Available

– Less Data at Filing with solicited updates (amendments)

FDA Resource Constraints

Limited Scientific Staff Prior to GDUFA

– Prioritization

Single Scientist Assessment Approach

– Delegation/Split Assessments

Changes in PEPFAR ANDA Assessments compared with the current OPQ Aligned Team approach under GDUFA

Early PEPFAR / Pre-GDUFA	Current PEPFAR / GDUFA
Single assessor process	Team-based assessment approach*
Prioritization, no formal goal dates	Established Assessment Goal Dates**
Resource limited (backlog)	Resources greatly enhanced (no backlog)

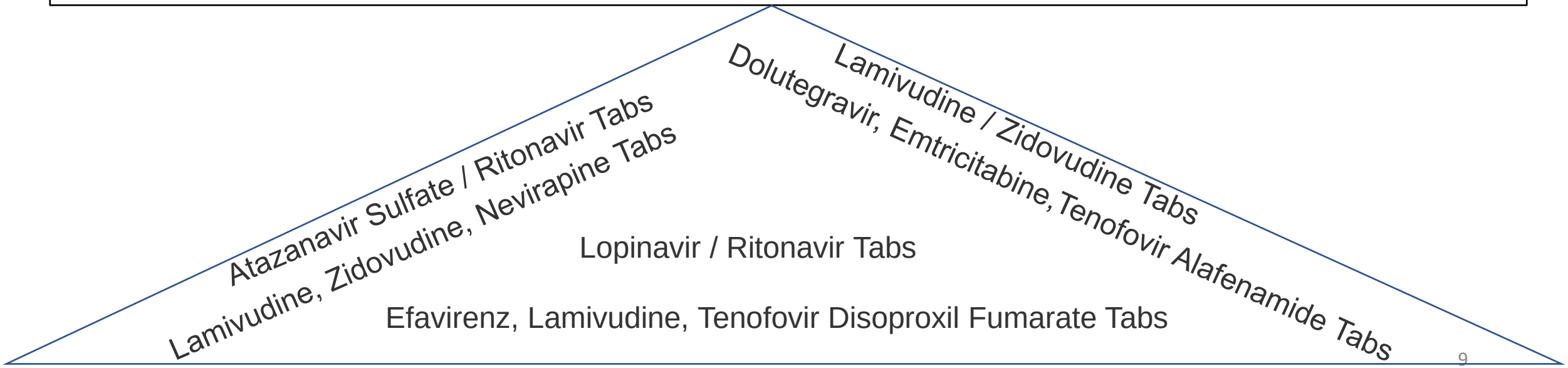
* **OPQ Aligned Team** -Drug Substance, Drug Product, Manufacturing Process, Biopharmaceutics, Project Manager

** PEPFAR Prioritization still exists under GDUFA

Current Priorities for PEPFAR Drug Product Quality Assessment – Reaching Tentative Approval

We continue to move PEFAR ANDAs toward **Tentative Approval Status**

- Focus on "Combo" products – contain more than one active pharmaceutical ingredient
  - Increased complexity
    - potential interactions between actives and/or excipients
    - impurity/degradant issues



Current Priorities for PEPFAR Drug Product Quality Assessment – Post Tentative Approval

Maintaining Tentative Approval Status when *Minor Changes* are made

- Increasing drug product shelf life, typically beyond 24 months

- Increasing tablet count per bottle to minimize visits to doctor/pharmacist
  - Typically, 3-month (90 tablets/bottle) or 4-month (120 tablets/bottle) dosing

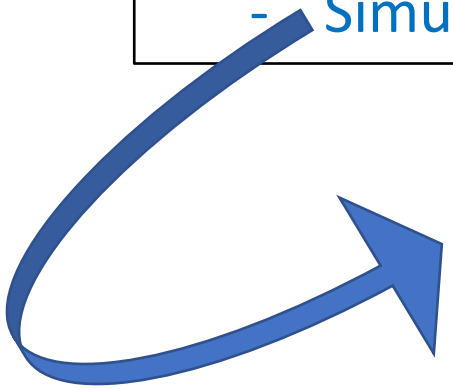
NOTE: For both cases above, we need assurance that product quality will be maintained for the patient.

Current Priorities for PEPFAR Drug Product Quality Assessment – Post Tentative Approval

Maintaining Tentative Approval status when *Minor changes* are made

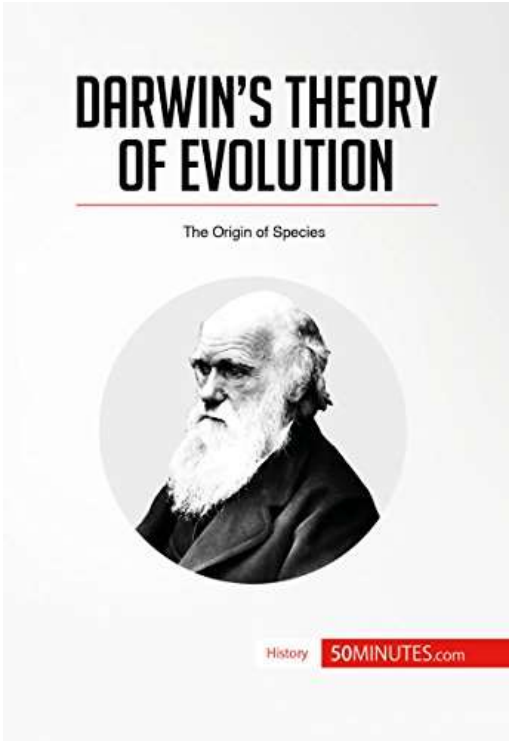
- Increasing drug product shelf life, often beyond 24 months
  - Additional stability data provided for assessment

- Increasing tablet count per bottle to minimize visits to doctor/pharmacist
  - Simulated "In-Use" Studies



- Repeated opening/closing of the bottle on a daily-basis with removal and testing of tablets to confirm that critical quality attributes are maintained under these conditions.

Summary of Drug Product Quality Assessment Considerations Under PEPFAR



We continue to adapt to urgent assessment needs, like the PEPFAR program, by improving our time to reach a decision on drug product quality…

…*without compromising* our quality standards that support that important, patient-centric decision.


Many Thanks